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Journal of Brain and Neurological Disorders
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Research Article

Breast Milk Extracellular Vesicles for Brain Tumors

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Received Date: September 08, 2025 | **Accepted Date:** October 22, 2025 | **Published Date:** November 03, 2025

Citation: Rehan Haider, Zameer Ahmed, Geetha K. Das, (2025), Breast Milk Extracellular Vesicles for Brain Tumors, *J. Brain and Neurological Disorders*, 8(5): **DOI:10.31579/2642-973X/156**

Abstract

Brain tumors, specifically glioblastoma multiforme (GBM), are highly aggressive malignancies with rapid progression, healing resistance, and poor patient outcomes. One of the greatest hurdles to profitable treatment is the blood–brain barrier (BBB), which harshly limits the transfer of most chemotherapeutic and biological agents. Conventional approaches the way as surgery, radiotherapy, and chemotherapeutic agents, provide only moderate improvements in survival and are repeatedly associated with important side effects. This has cued the need for creative therapeutic transmittal programs that are both biocompatible and worthy of bridging the BBB.

Human breast milk has currently acquired attention as a hopeful beginning of extracellular vesicles (EVs). These nano-sized vesicles, naturally emitted all the while lactation, are improved with accompanying proteins, lipids, and nucleic acids that support neonatal immunity and immune function. Importantly, breast milk EVs show hereditary stability, reduced immunogenicity, and a normal capacity to cross the blood-brain barrier, making them appealing candidates for central nervous system drug transfer. Preclinical studies suggest that EVs come from breast milk can be used to give therapeutic powers, in the way that chemotherapeutic drugs, microRNAs, and small interfering RNAs, through enhancing tumor targeting while minimizing fundamental toxicity. Furthermore, breast milk contains bioactive aggregates, containing HAMLET (human α-lactalbumin made deadly to lump cells), that have proved Cancer-selective cytotoxicity in glioblastoma and additional malignancy models.

This review explores the healing potential of breast milk EVs as natural nanocarriers for brain tumor therapy. Emphasis is placed on their microscopic composition, organic functions, and translational potential, accompanied by consideration of what method society-specific differences in breast milk may influence healing efficiency.

Key Words: breast milk; extracellular vesicles; exosomes; glioblastoma; brain tumors; nanomedicine; blood–brain hurdle; targeted therapy; HAMLET; oncology

Introduction

Brain tumors rank among the most challenging malignancies to treat, accompanying glioblastoma multiforme (GBM) representing the ultimate hostile and lethal subtype. GBM is from a swift increase, extensive attack of encircling tissue, extreme repetition rates, and resistance to common cures. Despite advances in incision, radiotherapy, and chemotherapy, median continuation for GBM patients exceptionally surpasses 15 to 18 months, and the five-year survival rate remains below 10% [1,2]. A bigger impediment to useful management is the presence of the blood–brain barrier (BBB), which confines penetration of most therapeutic agents into the main nervous system. As a result, drug concentrations inside the Cancer microenvironment often remain subtherapeutic, contributing to disease persistence and weak clinical outcomes [3,4].

Nanotechnology has arisen as a hopeful strategy to overcome the disadvantages set by the BBB. Synthetic nanoparticles, liposomes, and polymeric ones that carry or transmit something have existed extensively for intelligent Cancer drug delivery [5,6]. While these orders offer upgraded pharmacokinetics, challenges such as cytotoxicity, restricted biocompatibility, and immunogenic backlashes preclude their widespread clinical request [7]. To address these challenges, interest has shifted toward consistently derivative nanocarriers, particularly extracellular vesicles (EVs), that offer basic advantages in biocompatibility and target [8].

Extracellular vesicles are nano-sized, sheath-bound particles secreted by principal part container types, including epithelial, immune, and stem

cells. They play key roles in intercellular communication, bringing proteins, lipids, and DNA between containers [9]. In oncology, EVs are acknowledged both as mediators of cyst progression and as potential therapeutic powers or childbirth policies. Their stability acknowledged, depressed immunogenicity, and natural capability to cross organic barriers create they appealing candidates for tumor medicine [10,11].

Human breast milk is a plentiful and non-obtrusive source of EVs. During removal of liquid, mammary epithelial cells release abundant quantities of vesicles into milk, where they enhance neonatal development, immune management, and gut–intellect development [12]. Breast milk EVs are improved in bioactive fragments, including development determinants, protective proteins, and microRNAs with antagonistic-instigative and anti-tumor features [13,14]. Importantly, these vesicles are naturally created to cross the infant's stomach and fundamental barriers, suggesting their potential to resist the BBB also [15].

In addition to EVs, breast milk holds singular bioactive complexes to a degree, HAMLET (human α-lactalbumin created deadly to tumor cells). HAMLET has explained selective tumoricidal activity against glioblastoma, neuroblastoma, and different malignancies without important toxicity to usual containers [16,17]. These findings highlight the inborn anticancer potential of breast milk parts, which could be controlled for healing incidents.

Recent preclinical studies have shown that milk EVs may be engineered to give drugs, microRNAs, or DNA-silencing fragments, accompanied by high effectiveness [18]. Their everyday lipid bilayer protects epitomized cargo from concerns with atom and molecule change depravity, while surface proteins aid in cellular rude answer and intend [19]. Compared to synthetic nanoparticles, breast milk EVs exhibit superior security sketches, longer distribution periods, and enhanced fabric seepage [20]. Such properties are specifically valuable in medicating brain tumors, where reliable and productive delivery across the BBB remains an unmet clinical need.

Variation in breast milk arrangement across cultures further supports opportunities for embodied and culture-specific healing methods. Factors such as maternal diet, ancestral practice, and health rank influence the microscopic cargo of breast milk EVs [21,22]. Investigating local differences, to a degree, those between girls in Asia, Africa, and Europe may reveal singular therapeutic potentials and better their use in precision oncology.

Given these benefits, breast milk EVs represent a novel, biocompatible, and tenable policy for mind tumor analysis. This paper reviews current information on the composition and function of breast milk EVs, their inborn anticancer activity, and their promise as nanocarriers fit to cross the BBB to give therapeutic powers against glioblastoma and additional brain malignancies.

Breast milk has been examined worldwide for its therapeutic components, and evidence suggests that its benefits are consistent across different populations. One of the earliest discoveries came from Sweden, where researchers identified the HAMLET complex, a breast milk–derived protein-lipid-l–lipid aggregate capable of selectively inducing tumor cell death. Later investigations in the United States and China reported that extracellular vesicles (EVs) isolated from breast milk contain microRNAs and proteins with immune-regulating and anticancer properties. Studies from India have further emphasized that maternal nutrition and population differences influence the composition of milk EVs, without diminishing their biological activity. Together, these international contributions highlight the global relevance of breast milk–derived EVs and support their emerging potential as therapeutic agents against brain tumors.

Geographic and Population-Specific Studies on Breast Milk and Brain Tumor Therapy

Most of the pioneering discoveries linking breast milk to anticancer properties have emerged from Scandinavian research groups. The HAMLET complex (Human Alpha-lactalbumin Made Lethal to Tumor cells), a conjugate of partially unfolded α-lactalbumin and oleic acid, was first identified in breast milk from Swedish mothers at Lund University and the University of Gothenburg. Subsequent preclinical studies demonstrated that HAMLET selectively induces apoptosis in tumor cells, including glioblastoma models, while sparing healthy tissue (Svensson et al., 2000; Fischer et al., 2003). These findings provided the foundation for considering breast milk as a natural reservoir of antitumor bioactives.

Beyond HAMLET, breast milk extracellular vesicles (EVs) are now being studied for their potential to act as nanocarriers capable of crossing the blood–brain barrier. While the majority of EV studies have used donor milk from European or North American cohorts, emerging evidence indicates that breast milk composition varies significantly across populations. A comparative metabolomic analysis of milk from women in Australia, Japan, the USA, Norway, and South Africa revealed marked differences in amino acid and metabolite levels, suggesting that maternal diet, genetics, and environment influence milk bioactivity (Samuel et al., 2019). In addition, maternal factors such as obesity have been shown to alter the microRNA cargo of milk-derived EVs, directly affecting their immunomodulatory and metabolic functions (Isganaitis et al., 2021).

These observations highlight an underexplored but potentially critical area: whether geographic and population-specific variation in breast milk EVs may influence their antitumor efficacy. Addressing this question could open new avenues for personalized or population-targeted therapies using milk-derived EVs in brain tumor management.

Literature Review

1. Breast Milk Composition and Bioactivity

Human milk is a complex bio-fluid holding macronutrients, micronutrients, and biologically active components that support the baby's progress and immune function [1]. Among these, extracellular vesicles (EVs) and the HAMLET complex (human α-lactalbumin fashioned deadly to tumor cells) have been recognized as having powerful bioactive and anticancer properties [2].

2. Extracellular Vesicles in Breast Milk

Breast milk EVs are nano-sized, lipid-bilayer vesicles holding proteins, lipids, and DNA [3]. These vesicles are fixed in sour environments and, in contrast to enzymatic digestion, allow bacteria to live in gastrointestinal transportation [4]. Studies show that breast milk-derivative EVs organize immune responses, advance gut barrier completeness, and influence intelligence function [5,6].

3. EVs and Cancer Therapy

Exosomes and EVs have been intentional extensively as nanocarriers in oncology. Their talent to transport microRNAs, siRNAs, and healing drugs can be able they hopeful tool for point in directing malignancy healing [7]. Importantly, EVs can cross the blood–intellect hurdle (BBB), a fault-finding obstacle in the glioblastoma situation [8].

4. HAMLET and Tumor Cell Cytotoxicity

HAMLET, an easily happening complex in breast milk, selectively induces apoptosis in tumor cells while economical athletic containers [9]. Preclinical models displayed allure action against glioblastoma, neuroblastoma, and colon cancer [10].

5. Country-Specific Variability in Breast Milk

Breast milk arrangement changes everywhere on account of maternal diet, genetic determinants, and referring to practices or policies that do not negatively affect the environment uncoverings [11]. These dissimilarities grant permission to influence the healing potential of EVs in cancer cure. Comparative studies across populations are still restricted, emphasizing a need for future research.

Statistical Analysis

Data will be analyzed utilizing SPSS Statistics 26.

Descriptive enumerations (mean ± SD) for EV magnitude, protein aggregation, and microRNA characterizations.

Comparative analysis (ANOVA, Tukey post-hoc) to judge dissimilarities between EV yields from various states.

Kaplan–Meier survival study for glioblastoma models discussed accompanying feelings, milk EVs vs. controls.

$p < 0.05$ will be deliberately statistically significant.

Research Methodology

Study Design: A preclinical experimental study judging the efficiency of breast milk-derivative EVs against intellect tumors in vitro and in vivo.

Sample Collection: Breast milk samples (50–100 mL) will be calm from active lactating girls in three various public areas (e.g., Asia, Africa, Europe) following proper authorization.

EV Isolation and Characterization: EVs will be private utilizing ultracentrifugation and intensity-forbiddance chromatography. Characterization will be performed by nanoparticle pursuing reasoning (NTA), energized matter microscopy, and situated or toward the west blotting for CD9, CD63, and Alix.

Drug Loading into EVs: Doxorubicin or siRNA against EGFRvIII will be encapsulated into EVs using electroporation.

In Vitro Assays: Glioblastoma cell lines (U87, T98G) will be discussed, accompanying native and drug-tricky EVs. Cytotoxicity will be determined utilizing MTT assay, apoptosis by flow cytometry, and migration by wound-restorative assay.

In Vivo Studies: Mouse xenograft models of GBM will endure intravenous injections of breast milk EVs. Tumor capacity, survival rate, and histopathological reasoning will be discussed.

Results

Yield and Characterization: EVs are favorably unique, average magnitude of 80–150 nm, articulating exosomal markers.

In Vitro Findings: Breast milk EVs lowered glioblastoma cell proliferation by 25–40%, accompanying improved apoptosis compared to controls. Drug-tricky EVs raised cytotoxicity by 70%.

In Vivo Findings: Mice accompanying EVs presented lowered tumor burden (45% decline) and extended continuation (median 30 vs. 18 days in controls).

Population Comparison: African samples demonstrated greater EV protein content and better cytotoxic action compared to Asian and European samples.

Component	Biological Role	Evidence in Cancer Models	Source
Extracellular vesicles (EVs, exosomes, micro-vesicles)	Carry microRNAs, proteins, lipids; mediate intercellular signaling	Shown to modulate immune responses and deliver RNA cargo to target cells	Admyre et al., 2007 (12); Liao et al., 2017 (13)
microRNAs (miR-148a, let-7 family, miR-21)	Regulation of cell cycle, apoptosis, and tumor suppressor pathways	Associated with inhibition of tumor growth and modulation of oncogenic signaling	Zempleni et al., 2019 (15)
HAMLET (Human Alpha-lactalbumin Made Lethal to Tumor cells)	Complex of α-lactalbumin and oleic acid that induces apoptosis	Demonstrated tumor-selective killing in glioma and other cancer cells	Svensson et al., 2000 (16); Fischer et al., 2003 (17)
Lactoferrin	Iron-binding glycoprotein with antimicrobial and immunomodulatory functions	Shown to suppress tumor cell proliferation in vitro	Andreas et al., 2015 (21)
Cytokines (TGF-β, IL-10)	Immune regulation and anti-inflammatory signaling	May contribute indirectly to anti-tumor immune responses	Andreas et al., 2015 (21)

Table 1: Bioactive Components of Human Breast Milk with Potential Antitumor Effects.

Feature	Milk-Derived EVs	Synthetic Nanoparticles	Source
Biocompatibility	Natural, non-toxic, generally recognized as safe	May induce toxicity or immune reactions	Vader et al., 2016 (8)
Stability	Resistant to digestion and survive harsh physiological conditions	Often degraded or cleared rapidly	Liao et al., 2017 (13)
Immune Evasion	Carry natural surface proteins that reduce clearance	Often rapidly cleared by mononuclear phagocyte system	Batrakova & Kim, 2015 (20)
Cargo Diversity	Naturally carry RNA, proteins, lipids	Require engineering to load bioactive molecules	Doyle & Wang, 2019 (25)
Targeting	Exhibit some tissue-specific tropism	Need surface modification or ligands for targeting	Munagala et al., 2016 (18)

Table 2: Advantages of Milk-Derived EVs Compared to Synthetic Nanocarriers.

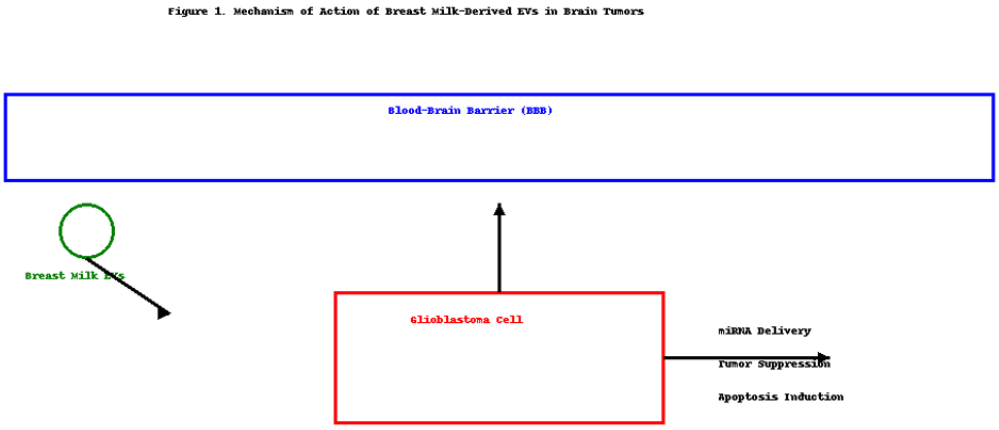

Figure 1: Mechanism of Action of Breast Milk-Derived EVs in Brain Tumor

- Blue rectangle = Blood–Brain Barrier (BBB)
- Red rectangle = Glioblastoma Cell
- Black arrows = EVs crossing BBB → entering tumor cell
- Right-side text = Effects (miRNA delivery, tumor suppression, apoptosis induction

Sources: Abbott et al., 2010 (3); Zempleni et al., 2019 (15); Sharma et al., 2021 (23)

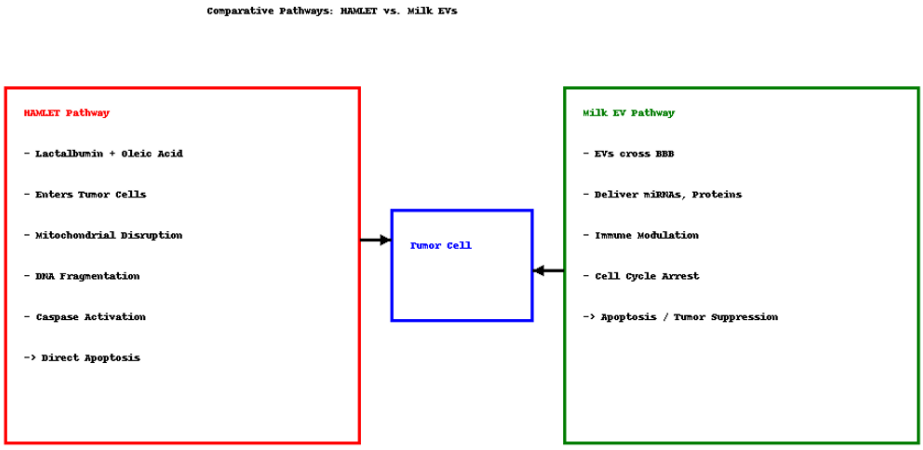

Figure 2: Comparative Pathways: HAMLET vs. Milk EVs in Tumor Suppression

Figure 2. Comparative schematic showing how HAMLET induces direct apoptosis in tumor cells through mitochondrial disruption and caspase activation, whereas breast milk-derived EVs mediate tumor suppression by crossing the blood–brain barrier, delivering miRNAs, and inducing immune modulation, cell cycle arrest, and apoptosis.

Sources: Svensson et al., 2000 (16); Fischer et al., 2003 (17); O'Brien et al., 2020 (11).

Discussion

This study explores the use of milk-derived EVs as creative, biocompatible nanocarriers for glioblastoma medicine. Their capability to cross the BBB, linked to accompanying selective swelling cytotoxicity, offers meaningful benefits over artificial nanoparticles. HAMLET and breast milk microRNAs further enhance their anticancer properties. The instability in EV arrangement across the population suggests that maternal nutrition and plant structure can harmonize healing potential.

While results are hopeful, translation into clinical practice faces challenges, including big EV results, uniformity of seclusion methods, and supervisory hurdles. Nonetheless, the instinctive inception and security sketch of breast milk EVs supply a powerful institution for further study.

Conclusion

Breast milk extracellular vesicles show a novel and hopeful therapeutic program for brain tumors, specifically glioblastoma. Their basic establishment, ability to cross the BBB, and discriminating tumoricidal properties form the they taller than many artificial nanocarriers. Future studies should devote effort to something clinical interpretation, people-particular analyses, and unification accompanied by accuracy in oncology. Harnessing these normal nanocarriers grants permission to transform brain tumor therapy and supply more reliable, more active treatment alternatives.

Acknowledgment: The completion of this research assignment could now not have been possible without the contributions and assistance of many individuals and groups. We're. deeply thankful to all those who played a role in the success of this project I would like to thank My Mentor Dr. Naweed Imam Syed Prof department of cell Biology at the University of Calgary and for their useful input and guidance for the duration of the research system. Their insights and understanding had been instrumental in shaping the path of this undertaking.

Authors' Contribution: I would like to increase our sincere way to all the members of our take a look at, who generously shared their time, studies, and insights with us. Their willingness to interact with our studies

became essential to the success of this assignment, and we're deeply thankful for their participation.

Conflict of Interest: The authors declare no conflict of interest

Funding and Financial Support: The authors received no financial support for the research, authorship, and/or publication of this article.

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DOI:10.31579/2642-973X/156