ABSTRACT

The therapeutic potential of peptide-based drugs is often constrained by formulation challenges, limited stability, and inefficient delivery mechanisms. This research aimed to address these unmet needs by developing advanced injectable and intranasal dosage forms for three clinically significant peptides: oxytocin (OXT), vasopressin (VP), and angiotensin (ANG). The overarching goal was to enhance therapeutic efficacy, improve patient convenience, and enable targeted delivery, particularly to the central nervous system (CNS).

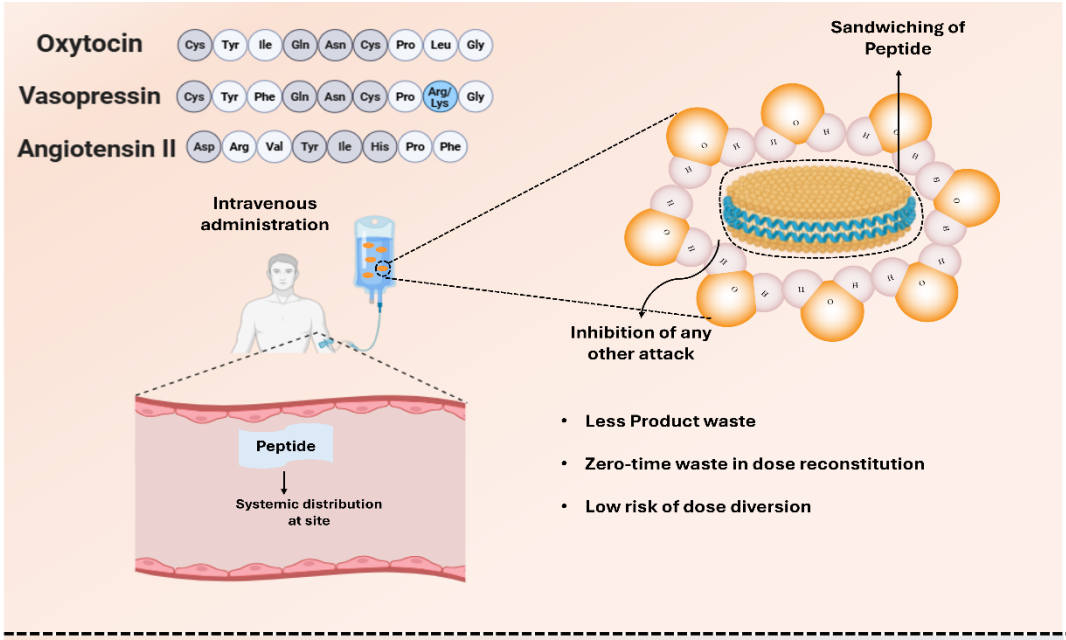
To achieve this, three distinct formulation strategies were employed:

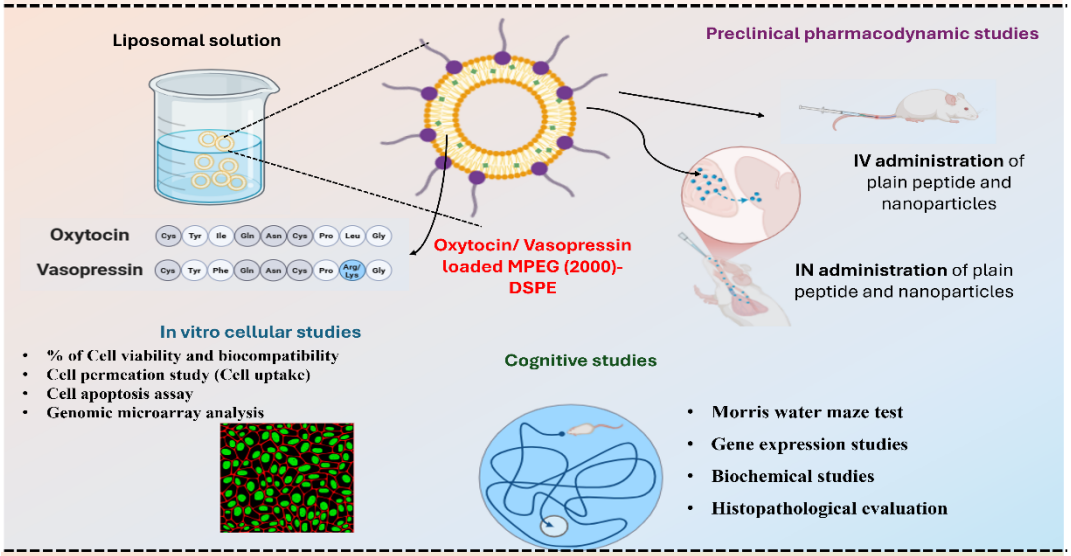
Ready-to-Infuse (RTI) Formulations: RTI dosage forms of OXT, VP, and ANG were developed for intravenous administration, eliminating the need for reconstitution prior to use. Each formulation was prepared at FDA-recommended strengths and characterized for critical quality attributes (CQAs), including sterility, stability, and potency. Stability studies conducted under ICH Q1E guidelines revealed extended shelf lives—up to 25.36 months for OXT, 36 months for VP, and 34.485 months for ANG when stored at 5±3°C.

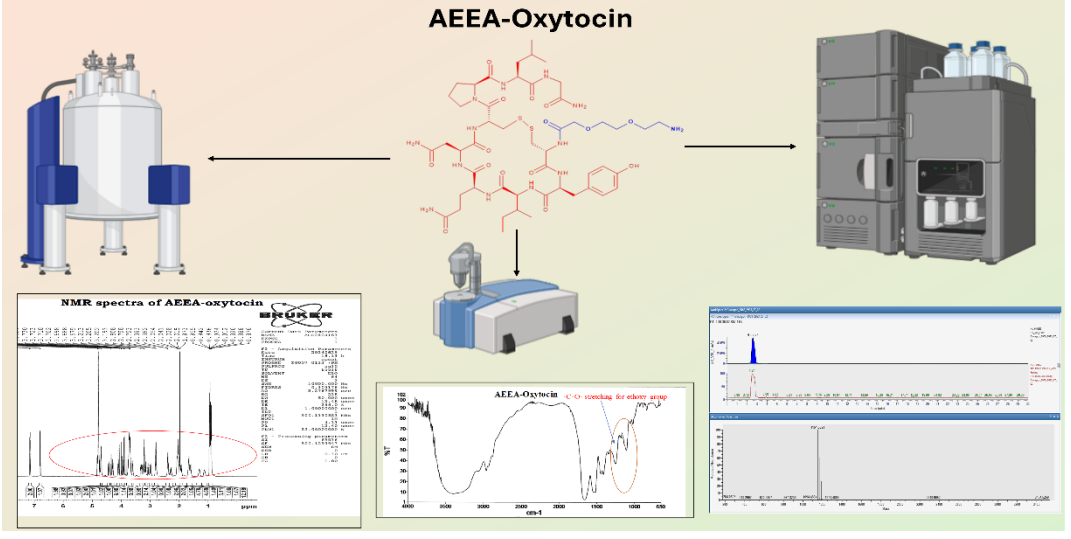
Lipidic Nanovesicle Technology: To facilitate nose-to-brain delivery, lipid-based nanovesicles were formulated for intranasal administration of OXT and VP. These systems were thoroughly characterized and evaluated through in vitro and preclinical studies, demonstrating significantly enhanced CNS targeting and therapeutic efficacy compared to conventional formulations.

AEEA Conjugation Strategy: A novel conjugation approach using aminoethoxyethoxy acetic acid (AEEA) was applied to OXT to further improve its cerebral delivery. The conjugate was validated using NMR, FTIR, and mass spectrometry, and its performance was assessed in a neurodegenerative animal model. Results confirmed improved brain permeation and favorable biopharmaceutical properties.

In conclusion, this research successfully demonstrated that RTI formulations, lipidic nanovesicle systems, and AEEA-based conjugation strategies can substantially enhance the physicochemical stability, delivery efficiency, and therapeutic potential of peptide drugs. These innovations offer promising avenues for clinical translation and improved patient outcomes in peptide-based therapies.


Oxytocin
Cys Tyr Ile Gln Asn Cys Pro Leu Gly
Vasopressin
Cys Tyr Phe Gln Asn Cys Pro Arg/Lys Gly
Angiotensin II
Asp Arg Val Tyr Ile His Pro Phe
Sandwiching of Peptide
Intravenous administration
Inhibition of any other attack
Peptide
Systemic distribution at site
Less Product waste
Zero-time waste in dose reconstitution
Low risk of dose diversion


Liposomal solution
Preclinical pharmacodynamic studies
Oxytocin
Vasopressin
Oxytocin/ Vasopressin loaded MPEG (2000)-DSPE
IV administration of plain peptide and nanoparticles
IN administration of plain peptide and nanoparticles
In vitro cellular studies
% of Cell viability and biocompatibility
Cell permeation study (Cell uptake)
Cell apoptosis assay
Genomic microarray analysis
Cognitive studies
Morris water maze test
Gene expression studies
Biochemical studies
Histopathological evaluation


AEEA-Oxytocin
NMR spectra of AEEA-oxytocin
BRUKER
AEEA-Oxytocin