Original Article

Development of Carmustine Loaded PLGA-PEG Conjugates for Nose to Brain Targeting

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ABSTRACT

Intranasal drug delivery is a promising route for drug delivery directly to the brain for acute or chronic treatments. A direct route to the brain offers a rapid approach to delivering drugs to the central nervous system without using the parenteral route. Carmustine is a nitrosourea used to treat brain tumors, multiple myeloma, lymphoma, and Hodgkin's disease but its use is limited by a very little half-life in the body fluids. The nanoparticles have shown great potential to overcome problems related to shorten shelf life. The present study aims to develop a nose-to-brain delivery system for Carmustine to prevent degradation and prolong it's bioavailability at the target site. It has shown that the nanoparticles have uniform size and shape and were found to be 231 ± 21.2 nm with 0.128 PDI. The system has stabilized with sufficient surface charge and the zeta potential of the system was found to be -21.2 ± 2.3 mV. After 24 h, cumulative drug release from the prepared system was found to be the maximum release of around 96.69 ± 3.38 in the phosphate buffer pH 6.8.

Keywords: Nose-to-Brain delivery, Nanoparticles, Carmustine, Emulsification Solvent, Evaporation Method.

INTRODUCTION

The World Health Organization (WHO) estimates that 35% of diseases in Europe are brain disorders.[1] Neurodegenerative, cerebrovascular, and cancerous illnesses are the most prevalent neurological c1onditions. However, only 5% of the over 7000 drugs in the comprehensive medicinal chemistry, treat brain diseases, mainly sadness, schizophrenia, persistent agony, and epilepsy.[2-3] Most of these drugs require an improvement in their penetration into the brain. More than 98% of small drugs never reach the brain, which is true for almost all large drugs.[2] This discouraging circumstance is due to the brain's structure, adverse reactions, and the blood-brain barrier's impenetrability (BBB) and blood-cerebrospinal fluid barrier (BCB).

Nanocarriers have emerged as one of the most promising candidates for drug delivery due to their target-specific controlled drug release, biocompatibility, surface modification, and encapsulation of diverse, active molecules, including drugs, peptides, genes, and vaccines.[4] To facilitate the provision of beneficial drugs towards the brain, pharmaceutical manipulation, disruption of the brain barriers, and other methods involving nanocarriers are being utilized. Intranasal drug delivery offers an alternative to the parenteral route for direct delivery to the brain for acute and chronic treatments.[5] Moreover, non-invasive method of administering drugs via intranasal administration with minimal systemic exposure to drugs, results in fewer toxic effects and better patient compliance.[6] Carmustine (CRM), a nitrosourea is used to treat brain tumors, multiple myeloma, lymphoma and Hodgkin's disease.[7-8] Besides, higher volume of distribution, it rapidly metabolizes after intravenous administration with a plasma half-life of 29 min.[9] Therefore, the present study aims to

Submission Date: 25-03-2022;
Revision Date: 10-06-2022;
Accepted Date: 10-08-2022.

DOI: 10.5530/ijper.56.4.188

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