CHAPTER 13

Strategies-Based Intrathecal Targeted Drug Delivery System for Effective Therapy, Modeling, and Controlled Release Action

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1. INTRODUCTION

According to WHO, approximately one in six of the world's population, suffer from central nervous system (CNS) disorders such as depression, seizures, locked-in syndrome, meningitis, and migraine. Despite multiple delivery routes for the targeted action to CNS, brain, and spinal are considered to be the most effective ways for emergency treatment. The presence of unique protective semipermeable layer composed of endothelial cell known as blood-brain barrier (BBB) acts as a challenging aspect for the delivery of actives to CNS. Intrathecal drug delivery has emerged as an alternative method for transportation to CNS, due to the direct administration to brain and spinal cord leading to the penetration through BBB and avoidance of side effect to other parts of the body. Intrathecal is the fluid-filled space present between the thin layers of tissue in the brain and spinal cord. Intrathecal drug therapy (ITDT) consists of a catheter connected with the drug reservoir for effective action from chronic intrathecal pain associated with osteoarthritis, fibromyalgia, shingles, and cancer [1]. ITDT aims to administer the drug directly to its receptor sites in a sufficient quantity for effective treatment and avoidance of adverse effects. The majority of patients for noncancer-related pain usually show spine pathologies as the cause of their pain. In cancer patient cases, intrathecal delivery of opioids are considered as an active mode for providing analgesic action with lesser side effects and higher quality of life. US FDA (United States Food and Drug Administration) approved the first battery-powered and programmable intrathecal pump for cancer-related pain in 1988 [2]. Table 1 shows the FDA-approved intrathecal preparations. The conventional dosage forms such as Rexulti, Brintellix, Trintellix, and Cipralex Meltz undergo first-pass metabolism leading to low amount of actives available for the therapeutic effect. Although ITDT provides the advantage of direct delivery to the targeted site, the procedure to deliver the active therapeutics remains complex. Nanotechnology is considered as a foremost strategy to overcome the drawbacks associated with conventional dosage form. Recent trends in nanotechnology show higher lipid solubility, physical stability of nanoparticle, drug loading, and controlled rate of release for enhancing the permeation of drug into lipid layers of brain fluid. Recent trends in ITDT include novel drug delivery systems such as peptide-based drug delivery, magnetic drug delivery system, and hydrogel-based drug delivery system. In peptide-based drug delivery, the drug is chemically conjugated by a linker to the targeted moiety by a specific receptor and undergoes endocytosis to improve the delivery of drug. A novel approach of intrathecal magnetic drug targeting is developed in a combination of traditional intrathecal drug administration with magnetic drug targeting for highly localized treatment of neurological disorders such as Arnold-Chiari malformation and non-complex regional pain syndrome (CRPS) neuropathic pain. Thus nanotechnology in ITDT shows effective therapy in pain management for patients suffering from chronic intractable pain conditions. So the objective of this article is to provide the insights of new strategies for the delivery of drug by intrathecal route and the new trends in this field of medicine.

1.1. Outline of the Chapter

This chapter is organized in four sections: Section 1 consists of the Introduction to ITDT and the difficulties

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