

## Drug Delivery in Central Nervous System Diseases - Technologies, Markets and Companies

**Description:** The delivery of drugs to central nervous system (CNS) is a challenge in the treatment of neurological disorders. Drugs may be administered directly into the CNS or administered systematically (e.g., by intravenous injection) for targeted action in the CNS. The major challenge to CNS drug delivery is the blood-brain barrier (BBB), which limits the access of drugs to the brain substance.

Advances in understanding of the cell biology of the BBB have opened new avenues and possibilities for improved drug delivery to the CNS. Several carrier or transport systems, enzymes, and receptors that control the penetration of molecules have been identified in the BBB endothelium. Receptor-mediated transcytosis can transport peptides and proteins across the BBB. Methods are available to assess the BBB permeability of drugs at the discovery stage to avoid development of drugs that fail to reach their target site of action in the CNS.

Various strategies that have been used for manipulating the blood-brain barrier for drug delivery to the brain include osmotic and chemical opening of the blood-brain barrier as well as the use of transport/carrier systems. Other strategies for drug delivery to the brain involve bypassing the BBB. Various pharmacological agents have been used to open the BBB and direct invasive methods can introduce therapeutic agents into the brain substance. It is important to consider not only the net delivery of the agent to the CNS, but also the ability of the agent to access the relevant target site within the CNS. Various routes of administration as well as conjugations of drugs, e.g., with liposomes and nanoparticles, are considered. Some routes of direct administration to the brain are non-invasive such as transnasal route whereas others involve entry into the CNS by devices and needles such as in case of intrathecal and intracerebroventricular delivery. Systemic therapy by oral and parenteral routes is considered along with sustained and controlled release to optimize the CNS action of drugs. Among the three main approaches to drug delivery to the CNS - systemic administration, injection into CSF pathways, and direct injection into the brain - the greatest developments is anticipated to occur in the area of targeted delivery by systemic administration.

Many of the new developments in the treatment of neurological disorders will be biological therapies and these will require innovative methods for delivery. Cell, gene and antisense therapies are not only innovative treatments for CNS disorders but also involve sophisticated delivery methods. RNA interference (RNAi) as a form of antisense therapy is also described.

The role of drug delivery is depicted in the background of various therapies for neurological diseases including drugs in development and the role of special delivery preparations. Pain is included as it is considered to be a neurological disorder. A special chapter is devoted to drug delivery for brain tumors. Cell and gene therapies will play an important role in the treatment of neurological disorders in the future.

The method of delivery of a drug to the CNS has an impact on the drug's commercial potential. The market for CNS drug delivery technologies is directly linked to the CNS drug market. Values are calculated for the total CNS market and the share of drug delivery technologies. Starting with the market values for the year 2012, projections are made to the years 2017 and 2022. The markets values are tabulated according to therapeutic areas, technologies and geographical areas. Unmet needs for further development in CNS drug delivery technologies are identified according to the important methods of delivery of therapeutic substances to the CNS. Finally suggestions are made for strategies to expand CNS delivery markets. Besides development of new products, these include application of innovative methods of delivery to older drugs to improve their action and extend their patent life.

Profiles of 74 companies involved in drug delivery for CNS disorders are presented along with their technologies, products and 74 collaborations. These include pharmaceutical companies that develop CNS drugs and biotechnology companies that provide technologies for drug delivery. A number of cell and gene therapy companies with products in development for CNS disorders are included. References contains over 400 publications that are cited in the report. The report is supplemented with 51 tables and 9 figures.

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