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Neurodegenerative diseases – understanding their molecular bases and progress in the development of potential treatments.

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Streszczenie

Neurodegenerative diseases such as Parkinson's, Alzheimer's, and prion diseases have at least three common denominators: (i) progressive loss of neuron function, which leads to cognitive decline; (ii) the molecular basis of the disease, which involves metalloprotein misfolding and aggregation (amyloid beta, alpha synuclein, and prion protein), or metal ion (Cu^{2+}, Zn^{2+}, and Fe^{3+}) imbalances that result in oxidative stress; and (iii) the current lack of a therapy to reverse or stop the progression of symptoms. These problems are discussed collectively in the present review. First, the molecular bases of these three diseases are explained in brief, with a special focus on the role of coordination chemistry in each case. Next, several commercial drugs that can be used to treat the symptoms are presented, i.e., those that do not aim to achieve metal ion homeostasis, which may be less well known in the bioinorganic community; and those that aim to achieve metal ion chelation, including the molecular scaffolds of those currently in clinical trials and the most promising targets that are still being studied in vitro. Another very important issue summarized in this review encompasses the strategies that have been developed to overcome the blood–brain barrier (BBB) and deliver drugs inside the brain. The BBB is a major obstacle in the development of drugs for treating central nervous system diseases. The BBB includes anatomical, physicochemical, and biochemical mechanisms that control the exchange of molecules between the blood and brain, thereby making the BBB virtually impermeable to drugs that might be used to treat neurodegenerative diseases. The non-optimistic nature of this review has a dual role. First, we present a true picture of the progress in the development of potential therapeutics. Second, we aim to encourage further targeted research in this area.

Słowa kluczowe

Neurodegeneration, metal ions imbalance, possible treatment

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