

## Current Trends in Therapeutics Research for Alzheimer's Disease

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Recent trends in research for Alzheimer's disease therapeutics are very promising. Currently, a multi-pronged approach is being adopted and many novel strategies are being explored. The eventual goal is to reduce the symptoms by improving neurotransmission in the brain, which slows down disease progression. Scientists are trying to block  $\beta$ -amyloid plaque formation using monoclonal antibodies (mAbs) by harnessing the power of the immune system. This helps to prevent clumping of the neurofibrils constituting the plaques, as well as clearing the  $\beta$ -amyloid plaques from the brain. In the last couple of years, several mAbs, including aducanumab and lecanemab have been approved by the USFDA for treating Alzheimer's disease. These mAbs are capable of removing  $\beta$ -amyloid plaques from the brain. The latter has been reported to reduce cognitive decline by 27% in patients with cognitive dysfunction arising from Alzheimer's. It is encouraging to note that lecanemab may hit the markets later this year. Also, several drugs have been repurposed to treat Alzheimer's disease. For example, the anticancer drug, saracatinib, is currently being tested in a murine model of Alzheimer's disease. This drug improved neurotransmission by restoring the function of the synapses. As a result, this restored the memory in these mice. Production blockers are another class of drugs that reduce the severity of Alzheimer's by blocking the production of  $\beta$ -amyloid plaques. There are two types of drugs in this class – the  $\beta$ -secretase inhibitors and the  $\gamma$ -secretase inhibitors. The latter have been found to be superior in clinical trials, as they exhibit lesser side effects and halt cognitive decline much more effectively than the  $\beta$ -secretase inhibitors. Another therapeutic

strategy is targeted at inhibiting tau-induced tangling of neurofibrils, which halts the formation of  $\beta$ -amyloid plaques. In order to stop the formation of tangles, a dual approach is being adopted, which use tau aggregation inhibitors and vaccines. Reducing brain inflammation in Alzheimer's patients is another goal of scientists. In this regard, a drug called sargramostim is currently being evaluated in clinical trials. Scientists are leaving no stones unturned. They are also exploring the possible link between the heart and the brain. This stems from the fact that heart health has been found to influence brain health. A study has indicated that estrogen-based hormone therapy decreases the chances of dementia and memory loss in post-menopausal women at higher risk of developing Alzheimer's disease. Unfortunately, the study didn't yield any conclusive results.

The future of Alzheimer's disease therapeutics could witness a sea of change. It is quite possible that combination therapies may be adopted, similar to the multi-drug regimens used to treat TB, HIV/AIDS, and cancer. Since drug development is a long, arduous, and expensive process, usually taking over a decade to develop and costing over \$350 million for a single drug, efforts are underway to accelerate the process. One such initiative is the Coalition against Major Diseases (CAMD). This coalition involves public-private partnerships and experts are optimistic that it will go a long way in expediting the process for developing affordable and effective therapeutics for Alzheimer's disease in the foreseeable future.

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