

# ACETYLCHOLINESTERASE INHIBITORS

**It is estimated that by 2050, 19 million people in the more developed countries will be over 65 years old. At least 50% of them are expected to develop some form of Alzheimer's disease.**



Source: www.sxc.hu

Research into potential targets



Preclinical research

Clinical research

Registration

Market

▶ Drug

## Description

Semi-synthetic derivatives of plant extracts that act as acetylcholinesterase (AChE) enzyme inhibitors. They can be used for the treatment of degenerative neuropathies such as Alzheimer's and Parkinson's diseases, as well as other disorders related to cholinergic transmission, such as *Myasthenia gravis*, chemical-related muscle paralysis, scopolamine intoxication, and other pathologies associated with memory loss.

## Problem

Alzheimer's disease (AD) is a disorder with a high socioeconomic impact, accounting for 1.70% of deaths in developed countries. It is estimated that 24.3 million people are affected and that 4.6 million new cases will be reported each year (WHO, 2005).

Alzheimer's is the fifth leading cause of death in developed countries, taking the lives of 168 thousand people per year (WHO, 2010).

In the U.S., 10.9 million people are unpaid caregivers. Most of these caregivers are close relatives of the patient, which causes a heavy emotional and financial burden on families as the disease progresses, ending in death. From the early symptoms to death, the progression of the disease is 8.5 to 11 years, with an average life expectancy of 4 to 6 years (Alzheimer's Assoc., 2010). The estimated global cost of treating Alzheimer's is approximately US\$ 315 billion (Pfizer®, Inc., 2009).

## Proposed solution

Inhibit the AChE enzyme to increase the cholinergic activity of the Central Nervous System, controlling the symptoms of Alzheimer's disease in the areas of learning and memory. Through this mechanism it is also possible to control muscle paralysis caused by chemical or biological agents, *Myasthenia gravis* and scopolamine poisoning.

## Benefits

The vegetable species in question is endemic to the Atlantic Forest and its extracted compounds may yield 4% in alcohol extract. In *in vivo* assays, these compounds have been found to inhibit the enzyme AChE completely (100%) when compared with the reversible inhibitor galantamine. They are also able to reverse amnesia induced experimentally by scopolamine, unlike tacrine and galantamine. The compounds do not present the toxic effects reported for the two commercial drugs used in preclinical testing.

## Market potential

In 2009, two of the main drugs for the treatment of Alzheimer's disease, rivastigmine and donepezil, both AChE inhibitors, reached sales of US\$ 954 million and US\$ 432 million, respectively. There is a high demand for new drugs, as indicated by the R&D lines on Alzheimer's of the major players in the pharmaceutical industry. In Brazil, the federal Exceptional Medicines Program and that of several state governments covers the costs of medications for pathologies such as Alzheimer's. The budget increase from 2004 to 2008 was 345%, corresponding to R\$ 2.3 billion last year.

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