

Oligomannate and Aducanumab: Novel Drugs for Alzheimer Disease

Dear Editor,

We read the article entitled “Nicotinamide Adenine Dinucleotide, the Sirtuins, and the Secret of a Long Health Span” on the esteemed “Ibnosina Journal of Medicine and Biomedical Sciences” with great interest. Anaizi reviewed the sirtuins, which is a family of proteins with broad enzymatic activities.^[1] Modifications in sirtuin activities have been associated with most age-related pathologies including Alzheimer’s disease (AD) and cardiovascular disease. Therefore, its study could provide new pathological pathways and new therapies improving the quality of life of individuals with cognitive decline.

AD is the most common type of dementia and may affect more than half of the population. In addition, it is among the most frequent causes of death because contributes to an increased risk of infection. AD is considered a neurodegenerative disease and it interferes in the spheres of cognitive functioning such as memory, attention, executive functioning, and language. The onset of AD typically is associated with age and normally presents with short-term memory loss and executive functioning. Functional and structural neuroimaging in AD are promising techniques to supplement the diagnosis and monitor the clinical course of the disease.^[2] The management of AD to date is only symptomatic including cholinesterase inhibitors and Partial N-Methyl D-Aspartate antagonists. In this context, donepezil (Aricept) was approved in 1996 and memantine in 2003 by the Food and Drug Administration.^[3] Here, our objective is to provide a comprehensible overview of two new drugs for AD. These medications are important because they have new promising mechanisms and are derived from different substances.

In China, an algae-derived drug called GV-971 (Oligomannate) indicated for mild to

moderate AD was approved in November 2019. It is extracted from an oligosaccharide marine alga and is the first novel drug approved for this disorder globally since 2003.^[4] The mechanism of the drug is in the microbiome found in the gastrointestinal tract. It is believed that a disbalance in the microbiota causes a misleading peripheral and central inflammatory process causing increase amyloid protein deposits and tau hyperphosphorylation. Hence, the algae-derived inhibits or decreases the development of this pathological pathway. GV-971’s III trial was done in a multicenter, randomized, double-blind, placebo-controlled, parallel-group, for almost a year, and more than 800 subjects with diagnosed mild-moderate AD were included. The results were promising and maintained throughout the study with a difference in the AD Assessment Scale-cognitive subscale of 2.54 ($P < 0.0001$) between the active drug group and placebo. However, some important facts to be highlight are that the study was only made in the Chinese population so studies in other populations are warranted. Moreover, the effect of the GV-971 is probably not equal for everyone because when the microbiome of the gut is analyzed there is a wide variation among individuals even in the same family.^[5,6]

Aducanumab is another drug under study, which is a recombinant human monoclonal antibody IgG1 κ targeting β -amyloid (A β). It is derived from the previously identified library of B cells collected from healthy elderly individuals with and without signs of cognitive impairment. The assumed mechanism of action of this drug is the targeting aggregated forms of A β , including soluble oligomers and insoluble fibrils deposited into the amyloid plaque in the brain of AD patients. In animal models, aducanumab entered the brain, bind parenchymal A β , and reduce soluble and insoluble A β in a dose-dependent manner.^[7] Aducanumab did not lead to the required results, but after further analysis with higher doses, resulting in a

significant reduction in the cognitive symptoms. More studies about aducanumab are therefore warranted and clinical trials are needed.^[8,9]

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Equal.

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Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

Ethical Approval not required

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REFERENCES

1. Anaizi N. Nicotinamide adenine dinucleotide, the sirtuins, and the secret of a long health span. *Ibnosina J Med Biomed Sci* 2020;12:8-22.
2. Rissardo JP, Caprara AL. Functional and structural neuroimaging in alzheimer's disease: An overview. *Hamdan Med J* 2020;13:132-3.
3. Kumar A, Sidhu J, Goyal A, Tsao JW. Alzheimer disease. In:

StatPearls. Treasure Island (FL): StatPearls Publishing; 2020. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK499922/>. [Last accessed on 2020 Sep 23].

4. Anderson P. Curiosity, Skepticism Over New Algae-Derived Chinese Alzheimer's Drug; 2019. Available from: <https://www.medscape.com/viewarticle/921319>. [Last accessed on 2020 Aug 25].
5. Wang X, Sun G, Feng T, Zhang J, Huang X, Wang T, *et al*. Sodium oligomannate therapeutically remodels gut microbiota and suppresses gut bacterial amino acids-shaped neuroinflammation to inhibit Alzheimer's disease progression. *Cell Res* 2019;29:787-803.
6. Seo DO, Boros BD, Holtzman DM. The microbiome: A target for Alzheimer disease? *Cell Res* 2019;29:779-80.
7. Falony G, Joossens M, Vieira-Silva S, Wang J, Darzi Y, Faust K, *et al*. Population-level analysis of gut microbiome variation. *Science* 2016;352:560-4.
8. Seigny J, Chiao P, Bussière T, Weinreb PH, Williams L, Maier M, *et al*. The antibody aducanumab reduces A β plaques in Alzheimer's disease. *Nature* 2016;537:50.
9. Anderson P. Aducanumab About-Face: Experts Weigh; 2019. Available from: <https://www.smedscape.com/viewarticle/920946>. [Last accessed on 2020 Aug 25].

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