Issue - 01

# Aoushadhavaani

A News Digest from Sri Adichunchangiri College of Pharmacy, ACU
comes to your hands monthly to update you with the latest news in healthcare sector.

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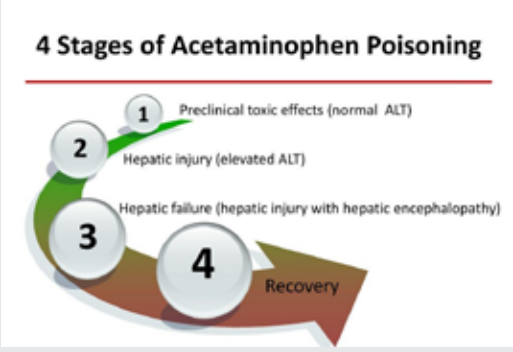
## Paracetamol Poisonings Up With High Doses




Poisonings related to paracetamol, or also known as acetaminophen, have gone up since the introduction of the high-dose formulation of 1,000 mg per tablet to the Swiss market, a study finds — raising alarms on the safety of high doses of this common pain killer.

For adults, the recommended maximum daily dosage is 4 grams. An overdose of paracetamol can lead to liver failure with fatal outcomes, or the requirement of a liver transplant.

Paracetamol is available in Switzerland in tablets of 500 milligram (mg) and 1,000 mg dosage. The latter dosage was introduced in 2003, and can be bought when prescribed by a physician, researchers from ETH Zurich have noted in their study.

In the cross-sectional study, the researchers reviewed 15,790 acetaminophen poisoning records and found a significant increase in reports of acetaminophen-related poisoning, in particular accidental poisonings, after the introduction of high-dose acetaminophen in 2003.

Among 42.1% of patients with follow-up information available, the incidence of poisoning with reported toxic doses of ≥10,000 mg was doubled after the introduction of high-dose acetaminophen compared with the period before (30.6% vs 15.3%).

Importantly, the researchers found that individuals using the

1,000 mg tablets were more likely to be exposed to potentially severe hepatotoxic doses of ≥10,000 mg than those using the 500 mg tablets (47.8% vs 17.8%).

Accordingly, accidental poisonings were significantly more common among users of 1,000 mg tablets than those taking 500 mg tablets (22.1% vs 11.0%).

Recently, experts have questioned the utility of acetaminophen in pain management, in view of the limited evidence of clinical benefits on conditions such as dental pain, headache, and musculoskeletal conditions.

The recent NICE guidelines, released in August 2020, has also removed acetaminophen (paracetamol) from chronic pain management, due to its unfavourable risk-benefit profile.

However, its use is on the rise despite accumulating safety concerns (for high doses) and limited evidence of benefit in pain management.

When the drug doesn't help to ease someone's symptoms, the people tend to increase the dosage without consulting a medical professional which is the real problem.n management is challenging, and other medications may have severe adverse effects. But, if paracetamol doesn't have the desired effect, it's important not to simply take more tablets. Instead, people should seek professional medical advice in order to find the best therapeutic option.

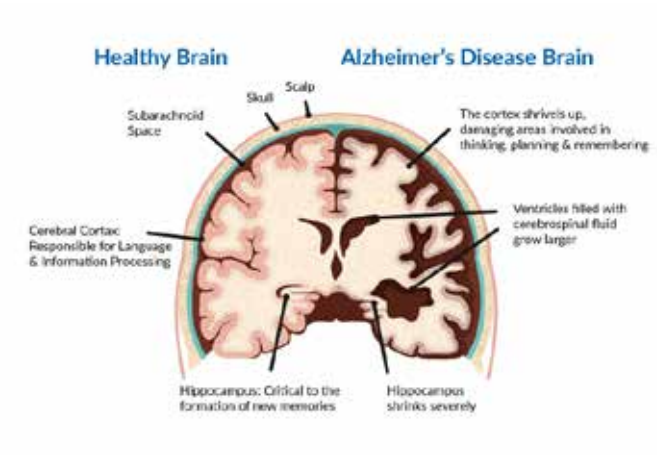
**For More Readings:**

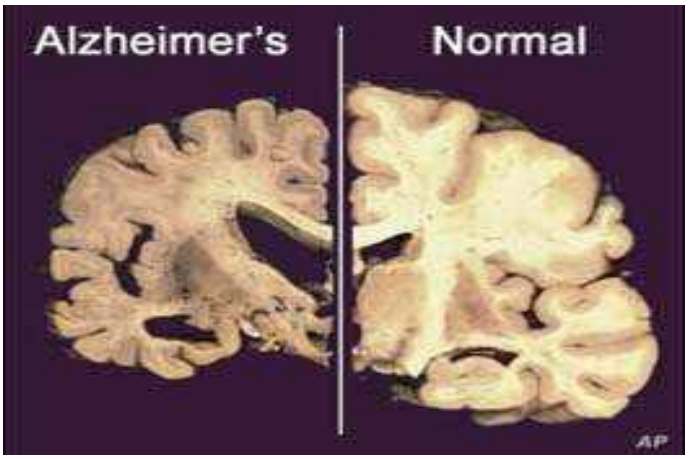
- https://specialty.mims.com/topic/paracetamol-poisonings-up-with-high-dose-tablets
- Clinical Practice Guidelines for Management of Paracetamol Poisoning in Children:- https:// www.rch.org.au /clinicalguide/guideline_index/Paracetamol_poisoning/
- Paracetamol Poisoning:- https://patient.info/doctor/paracetamol-poisoning
- Swiss study links higher-dosage paracetamol tablets to poisoning:- https:// theprint.in /health/ swiss -study -links-higher-dosage-paracetamol-tablets-to-poisoning/533371/

# Antidepressants in Alzheimer's Disease Prevention

According to recent evidence, the selective serotonin reuptake inhibitor (SSRI) "Escitalopram" holds promise in the prevention of Alzheimer's disease (AD), reducing amyloid-β-42 (Aβ42) levels in cerebrospinal fluid (CSF) and brain tissue in older adults with normal cognitive function, through serotonin (5-hydroxytryptamine [5-HT]) receptor subtypes 5-HT4, 5-HT6, and 5-HT7, to activate a signalling pathway that culminates in an upregulation of α-secretase activity to suppress Aβ42 generation.

A study was conducted among 114 cognitively healthy older adults aged 50–84 years where they receive either Escitalopram (20 mg daily for 2 weeks or 8 weeks, or 30 mg daily for 8 weeks) or placebo and measuring of Aβ levels in CSF samples collected using lumbar puncture before and after treatment.Compared with placebo, SSRI treatment resulted in a significant decrease in CSF Aβ42 .The combined Escitalopram doses produced an average reduction of 6.0% as opposed to a 3.5% increase noted with placebo. At the higher dose, Escitalopram was not able to remove existing plaques but completely hampered individual plaque growth over time.



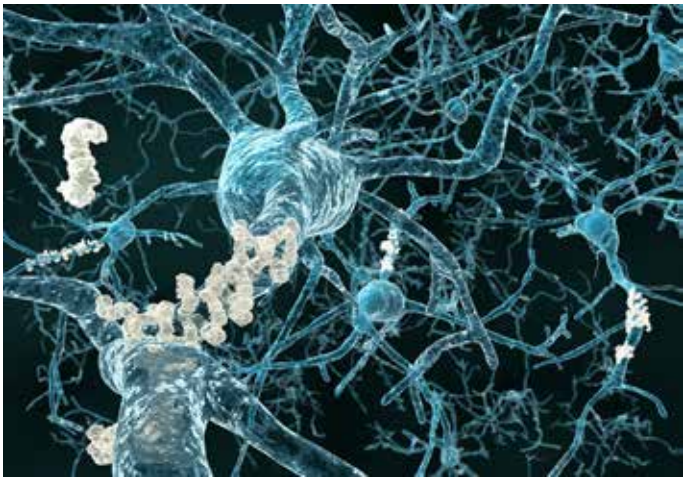

Although, reducing the rate of plaque accumulation is unlikely to be a viable treatment strategy for individuals who have already developed dementia, as there is little evidence that progression of their disease is dependent on the progression of their amyloid deposition, the results from this study have added new insights for the treatment modalities of Alzheimer's Disease.

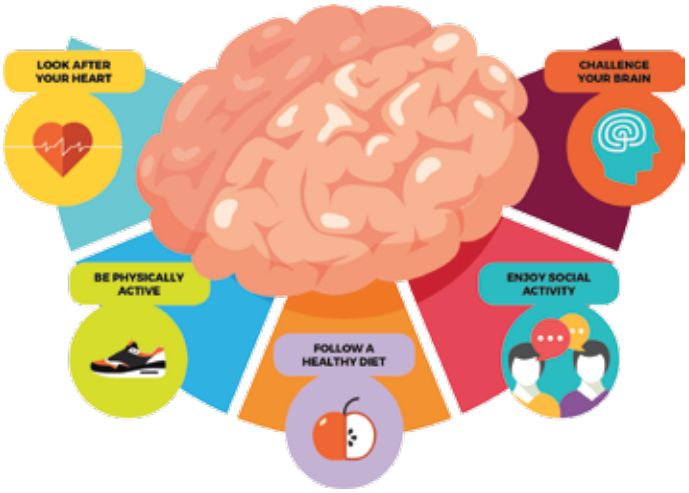
These findings are consistent with recent data from an Alzheimer mouse model, where a 4-month course of Escitalopram, administered via drinking water, reduced Aβ levels in the interstitial fluid of the brain by 25%. The authors attributed this reduction to an increase in α-secretase cleavage of amyloid precursor protein. (https://pubmed.ncbi.nlm.nih.gov/32913022/)

**"WHETHER YOU THINK YOU CAN, OR YOU THINK YOU CAN'T-YOU'RE RIGHT."**

- Henry Ford

On the contrary some studies, but not all, find that SSRIs neither do slow the course of AD nor improve the cognitive function of AD patients. To the extent that many people in the amyloid-negative group may never develop brain Aβ deposition it will be critical to determine how biomarker changes can be used to indicate a need for initiating treatment






However, it is still unclear whether the relatively modest reduction in CSF Aβ42 observed in cognitively healthy older adults could translate to clinical benefits. But if a greater reduction could be demonstrated for the higher 30-mg dose, or for a longer duration of exposure, or for a different SSRI more specific for the relevant 5-HT subtypes, the feasibility might be higher. However while considering the higher doses in geriatric population, caution is warranted given potential cardiac effects including increased QT interval.

**For More Reading:**

- https://specialty.mims.com/topic/alzheimer-s-disease-prevention--can-antidepressants-lend-a-hand-?topic-grouper=news
- Long-term treatment with certain antidepressants may reduce dementia incidence **:**https:// www.healio.com /news/psychiatry/20200828/longterm-treatment- with-certain-antidepressants- may- reduce- dementia-incidence.
- Interactions of Selective Serotonin Reuptake Inhibitors (SSRIs) with βAmyloid: https:// pubs. acs.org / doi/ 10.1021 /acschemneuro.8b00160

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