

Development of Multi Target Directed Chelates as a Drug Treatment for Alzheimer's Disease

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Background

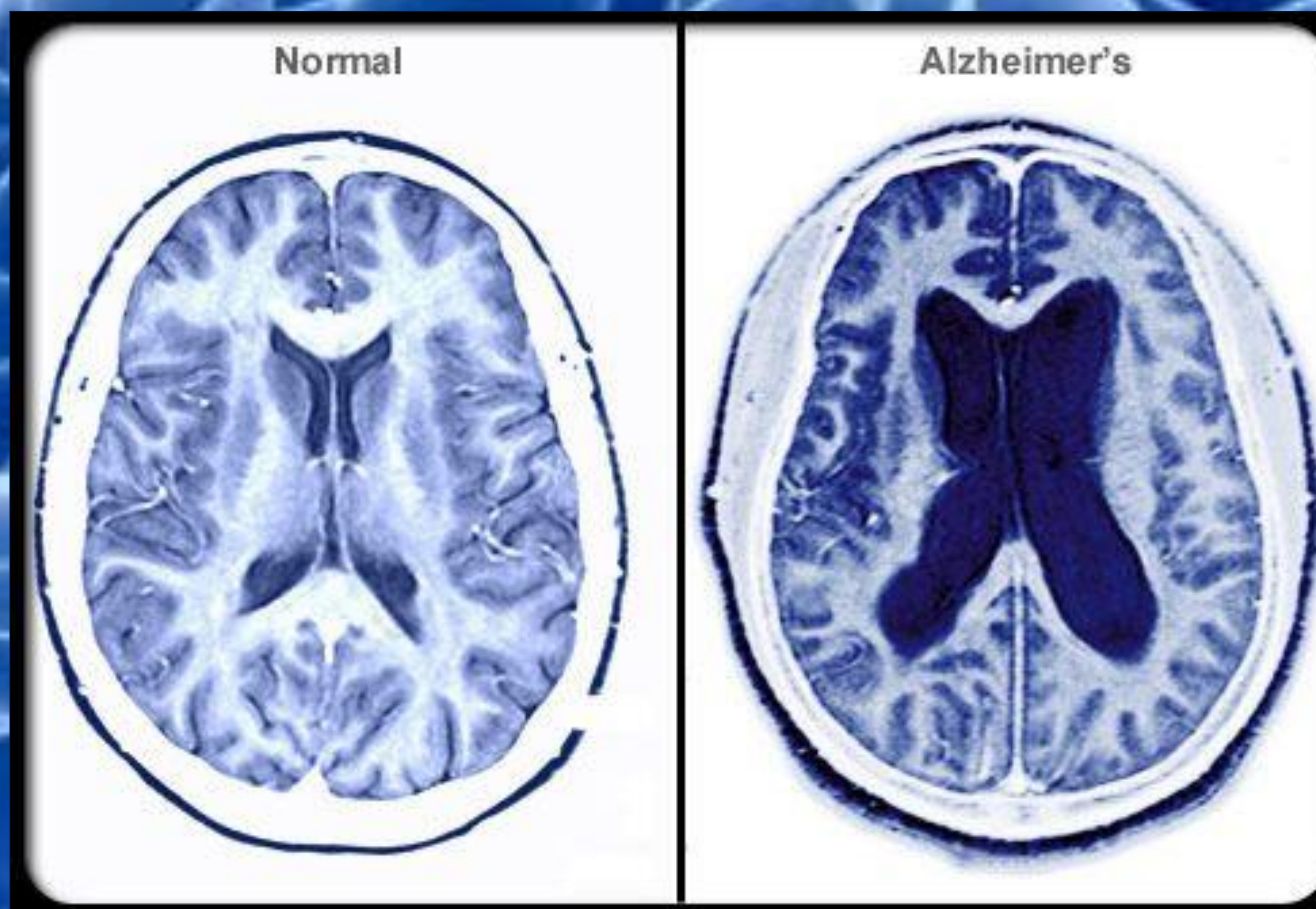
- Alzheimer's Disease (AD) is a form of dementia and is a neurodegenerative disease.
- It accounts for almost 80% of dementia cases, affecting no less than 50 million persons worldwide.
- The estimated global cost of AD is currently USD \$2 trillion.^[1]
- There are many Hypotheses regarding the pathogenesis of AD, this research focuses on four of these

The Hypotheses of AD ^[2]

Hypothesis	Suspected Role in AD
Amyloid	Over production and inadequate clearance of A β plaques
Cholinergic	Over activity of acetylcholinesterase and reduced acetylcholine levels
Metal Ion	Metal ion dyshomeostasis; Excess Fe ²⁺ , Zn ²⁺ , Cu ²⁺
Tau	Hyperphosphorylated Tau & Neurofibrillary Tangles

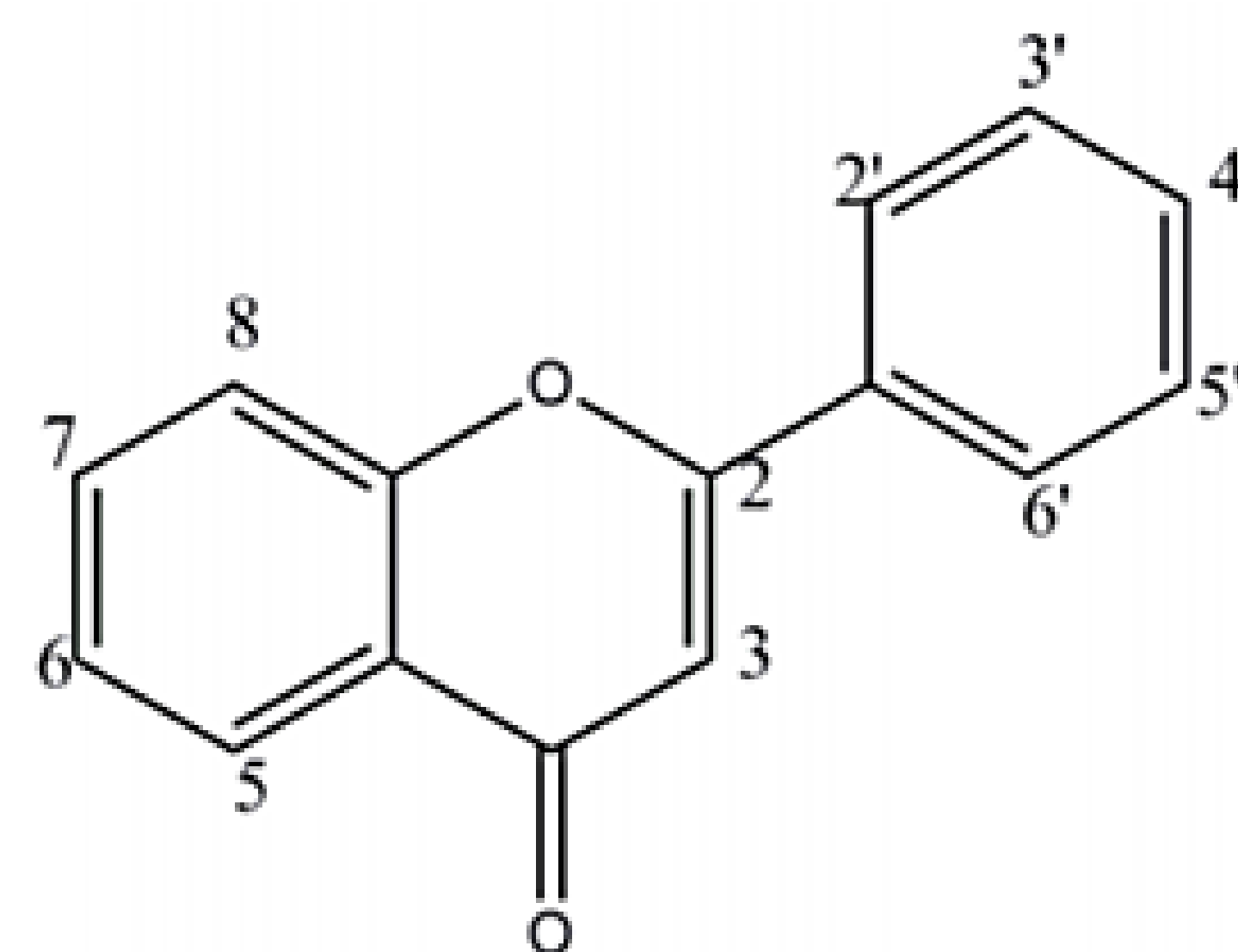
Aim

- To produce compounds that are expected to address the 4 hypotheses of interest.



Polymethoxy-substituted Anilines

- The choice of these anilines was inspired by the pharmacophores of methoxy-substituted flavones
- The pharmacophores have antioxidant, anti-cancer, anti-inflammatory properties ^[3]



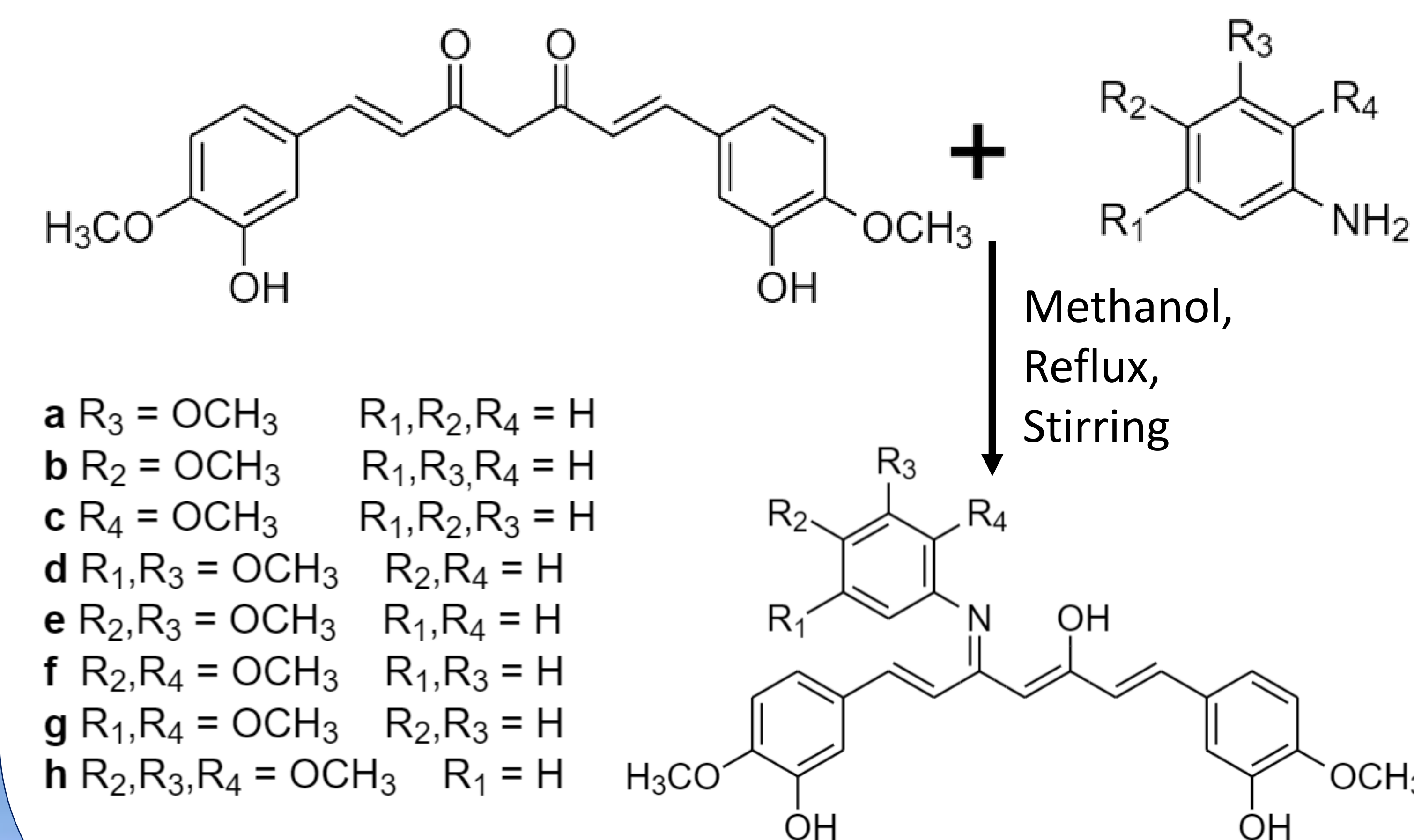
Methoxy groups on various positions on the prime ring are responsible for therapeutic properties toward AD: β -secretase inhibition and acetylcholinesterase inhibition^[3]

Curcumin

- Antioxidant with outstanding anticancer, anti-inflammatory and antibacterial properties.^[4]
- Improves cognition^[4]
- Inhibits Tau aggregation & β -secretase activity^[4]
- Can bind to A β and NFTs^[4]

Methodology Plan

- To synthesise novel derivatives of Curcumin using polymethoxy-substituted anilines in a simple reaction previously employed by Kareem *et al.* (2018)^[5]



[1] 2020 Alzheimer's Disease Facts and Figures. **2020**. Alzheimer's Dement.

[2] Agarwal, M., *et al.* **2021**. *J. Nanomater.*, 11(1), 1–18.

[3] Yao EC, Xue L. **2014** Adv Alzheimer Dis

[4] Ma QL, Zuo X, Yang F, *et al.* **2013** The Journal of Biological Chemistry

[5] Kareem, A. *et al.* **2018**. *J. Mol. Struct*