Nanoliposomes form of curcumin and miRNA for Alzheimer’s disease therapy

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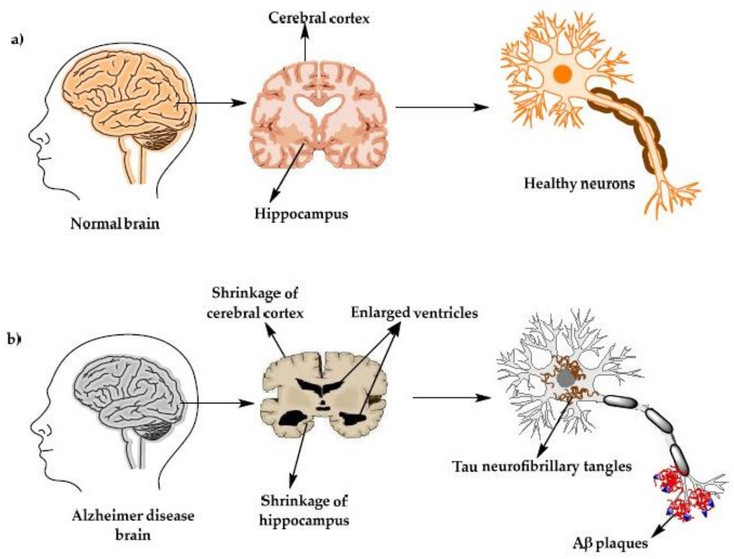
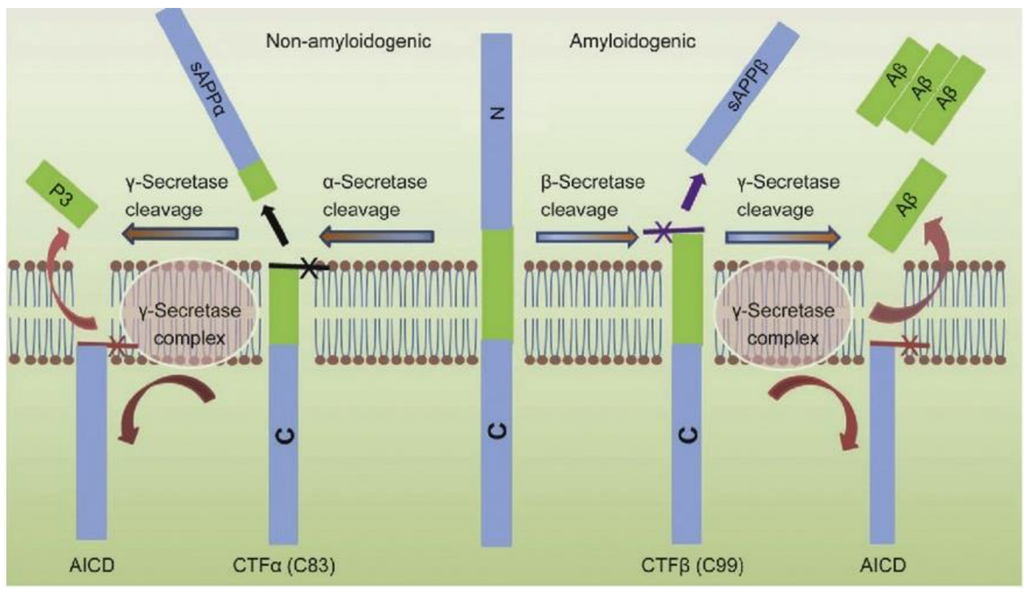
A large body of scientific research points to inflammation as a mechanism most often present in the development of Alzheimer's disease (AD). Curcumin targeted delivery may be a viable alternative to classical treatment protocols. The delivery system can be liposomes - universal systems that can be loaded with both lipophilic and hydrophilic compounds. Mixture of sunflower phospholipids in the form of powder (defatted dry lecithin) was used as a raw material for the formation of liposomes.

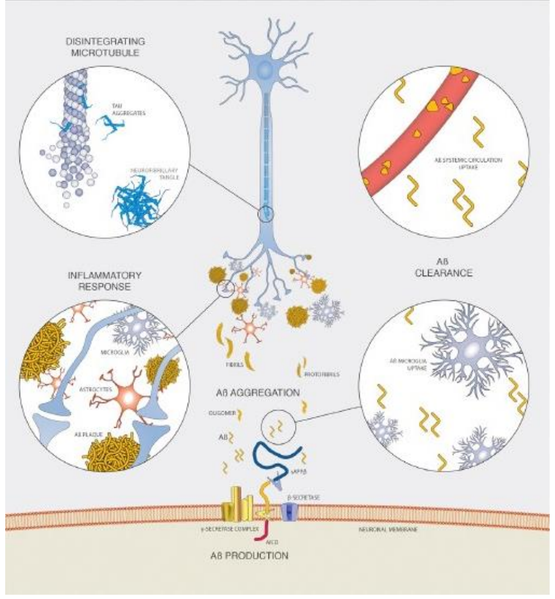
The aim. Development of a new drug – aerosol lipid target systems containing curcumin and microRNA (drug) for the treatment of neurodegenerative diseases. Determination of anti-inflammatory and anti-amyloid activity of the drug, its effectiveness in relation to the dose and duration of action and aftereffects in vivo.



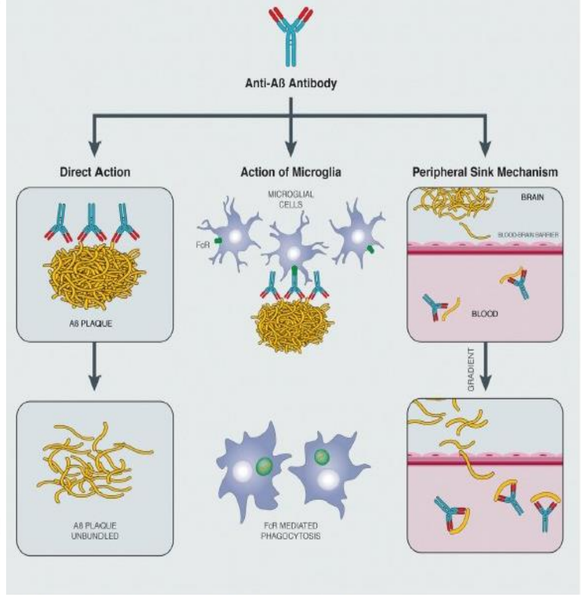
The physiological structure of the brain and neurons in (**a**) healthy brain and (**b**) Alzheimer’s disease (AD) brain [1].



Schematic structure depicting Aβ as the main aggregated component of amyloid plaques in the brain. The amyloidogenic pathway consists of the sequential cleaving of amyloid precursor protein (APP) by β-secretase, which releases the soluble ectodomain sAPPβ. The C99 fragment of APP is then cleaved by γ-secretase, resulting in the formation of the Aβ peptide. The Aβ peptide has a high tendency to accumulate, oligomerise, aggregate, and forms amyloid senile plaques, resulting in the substantiated alterations in Alzheimer’s disease [2]



Scheme of the amyloid-β (Aβ) cascade hypothesis in Alzheimer disease [3]



Mechanism of amyloid-β (Aβ) removal via Aβ-specific antibodies. FcR = Fc receptors [3]

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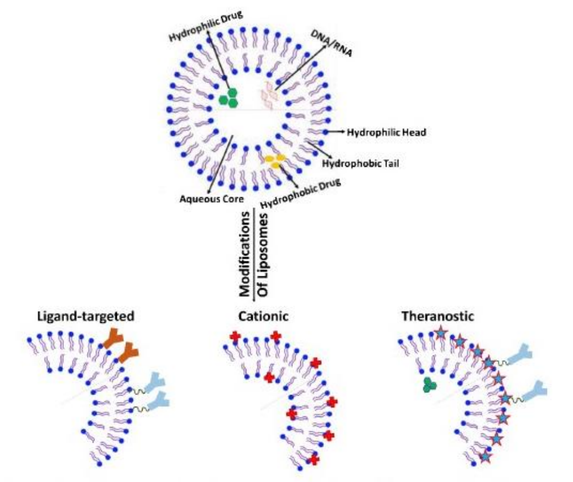
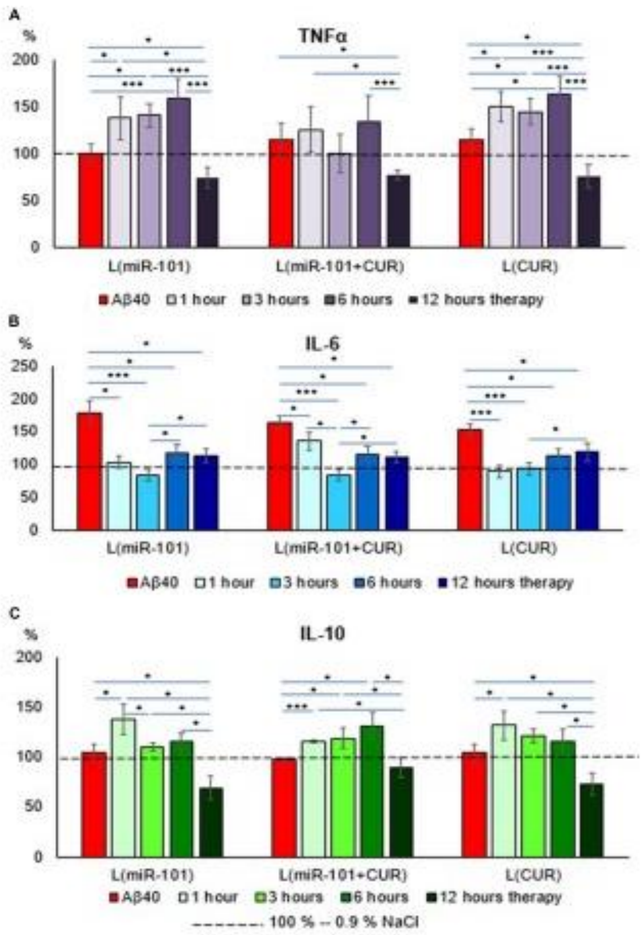
Phospholipids and their fatty acid composition were identified by tandem mass spectrometry. Liposomes were prepared by "freezing-heating" methods; "sonication" and extrusion. The most effective method for liposomal form of curcumin creating was determined. It was the extrusion through membranes method. Curcumin liposomal form obtaining method included dissolving a mixture of sunflower phospholipids, cholesterol, and polyethylene glycol and curcumin solution adding; evaporating of mixture until a lipid film was formed; hydration, and sequential extrusion through membranes with pore diameters of 200, 100, and 50 nm. The size of "empty" liposomes and liposomes with curcumin and microRNA was determined using: a) dynamic light scattering using a laser photocorrelation spectrometer and b) atomic force microscopy (AFM). The efficiency of curcumin encapsulation was 95.34 ± 3.76%.

The effect of curcumin on the expression of APP and Aβ in response to treatment with curcumin at different concentrations and the effect of curcumin on the expression of APP and Aβ from miRNAs were evaluated. Curcumin was shown to decrease mRNA, APP, Aβ40 and Aβ42 levels compared to untreated cells.



Basic structure of liposome and structural modification of liposomes for infiltration to brain [4].



Diagrams of the relative content of cytokines: TNFα (A), IL-6 (B), and IL-10 (C) in mononuclear cell suspension after 1 h of incubation with Aβ40 aggregates and subsequent incubation over time 1, 3, 6, and 12 h with liposomal forms of miR-101, CUR, and miR-101 + CUR. The vertical axis is the concentration of the corresponding cytokine in the target samples normalized to the corresponding concentration of this substance in the suspension of mononuclear cells incubated with saline, %. *P < 0.05, ***P < 0.001 [5].

The obtained data found the sunflower phospholipids using as raw material for the nano-sized containers creation – liposomes for pharmacologically active ingredients transport and strategy for the Alzheimer's disease treatment, taking into account the key role of the liposomal form of flavonoids and micro RNA.

References

1 Breijyeh, Zeinab; Karaman, Rafik (2020). *Comprehensive Review on Alzheimerâs Disease: Causes and Treatment. Molecules, 25(24), 5789* –. doi:10.3390/molecules25245789

2 Samuel C. Ugbaja;Zainab K. Sanusi;Patrick Appiah-Kubi;Monsurat M. Lawal;Hezekiel M. Kumalo; (2021). *Computational modelling of potent β-secretase (BACE1) inhibitors towards Alzheimer's disease treatment . Biophysical Chemistry, 270, 106536* –. doi:10.1016/j.bpc.2020.106536

3 Panza, Francesco; Lozupone, Madia; Seripa, Davide; Imbimbo, Bruno P. (2019). *Amyloid-β Immunotherapy for Alzheimer's Disease - Is It Now A Long Shot…?. Annals of Neurology, 85, 303-315* –. doi:10.1002/ana.25410

4 Hernandez C, Shukla S (2022) *Liposome based drug delivery as a potential treatment option for Alzheimer’s disease. Neural Regen Res 17(6):1190-1198* -. https://doi.org/10.4103/1673-5374.327328

5 Sokolik VV and Berchenko OG (2023) *The cumulative effect of the combined action of miR-101 and curcumin in a liposome on a model of Alzheimer’s disease in mononuclear cells. Front. Cell. Neurosci. 17:1169980* - doi: 10.3389/fncel.2023.1169980