

# Novel trends in the management of Alzheimer's disease by using Nano based Materials

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## Article Info

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## Abstract

Alzheimer's disease is a neurodegenerative disease of the brain, clinically there is a slowly progressive cognitive deterioration leading to devastating memory problems and incapability of performing learned actions like dressing or even taking bath. Wandering, aggression and psychotic behaviors are also the part of the spectrum. There are various treatments and diagnostics are available for this disease. Among these treatments and diagnostics, nanoparticle based approaches deserve special attention. When the size of the material comes with in the 100 nanometer range, according to quantum physics the materials begin to show remarkable novel properties. This study has been undertaken to highlight the promising ongoing developments in the diagnosis and management of Alzheimer's disease (AD) backed up by nanotechnology.

**Keywords:** Alzheimer's disease; Nanotechnology; Blood-brain barrier; Biomarker; Curcuminliposome; Nanoprobe.

## Introduction

Alzheimer's disease (AD) one of the major causes of dementia, is more or less still a clinical diagnosis by exclusion. Histologically there are beta-amyloid deposits and neurofibrillary tangles in the cerebral cortex, hippocampus and sub cortical gray matter ultimately leading to neuronal dysfunction and cell death of the affected area. Biochemically there is reduction in neurotransmitter acetylcholine. Actually cause is unknown and an effective treatment is yet to emerge. One of the main causes of dementia in AD is due to the neurodegeneration resulted by the increased beta-amyloid levels. The present treatment with acetyl cholinesterase inhibitor drugs(Donepezil, Rivastigmine, Galantamineetc) are not clinically very effective due to their poor solubility, lower bioavailability, and ineffective ability to cross the blood-brain barrier [1]. Blood-brain barrier (BBB) is formed by the endothelial cells lining of the cerebral vessels, and it protects brain from toxins and abrupt changes in plasma chemistry [2]. At the same time there is no rapid detection or monitoring modalities for AD as of now.

## Beta-Amyloid Peptides as Potential Biomarker

Beta-amyloid peptides are potential biomarker for monitoring and detecting AD in its early stage. According to Ajeet Kaushik, et al [3] Beta-amyloid ( $\beta$ -A) peptides are very useful biomarkers for AD at the point-of-care (POC) level. Detection of this by affordable nano enabled electrochemical biosensor device in the body fluids will be the feasible, non invasive method of the future<sup>3</sup>. Nano-enable biosensors can detect beta-amyloid at low levels. Such sensor can be developed for AD monitoring at point-of-care at its initial stage and it can be properly and effectively treated.

## Curcumin as MRI Contrast agent in detecting Alzheimer's disease

Curcumin, a common Indian spice used in curry powders has antioxidant, anti-inflammatory and lipophilic properties which improves the cognitive functions in patients with AD. A growing body of evidence indicates that oxidative stress, free radicals, beta amyloid, cerebral deregulation caused by bio-metal toxicity and abnormal inflammatory reactions contribute to the key event in Alzheimer's disease pathology [4]. Curcumin (CUR), effectively binds to beta-amyloid plaques and can cross blood brain barrier.

Dr. Rameshwar Patil et al [5] have designed a novel nanoimaging agent (NIA) based on nature-derived poly( $\beta$ -malic acid) (PMLA) containing covalently attached gadolinium-DOTA(Gd-DOTA) and nature-derived CUR. This NIA recognizes and selectively binds to beta-amyloid plaques and is detected by MRI. It efficiently identified beta-amyloid plaques in human and mouse samples by an ex vivo staining. Though Gadolinium based MRI contrasts thought to be safer, later proved to be causing nephrogenic systemic fibrosis (NSF) and many dyes do not cross blood brain barrier effectively for proper visualization.

### Therapeutic+Diagnostic=Theranostic

Theranostics is considered a natural marriage of molecular imaging and drug delivery technologies, the same targets described for imaging technologies are also potentially suitable for therapeutic purposes. Theranostics is a relatively new discipline in the context of personalized medicine, and involves use of nanotechnology to assemble molecular platforms that simultaneously perform a therapeutic and diagnostic function [6]. Nanotheranostic strategy has been successfully exploited in oncology and is now emerging as a possibility for Alzheimer's disease, Medicinal chemists do not yet completely understand the nuances of theranostic action and consequently have not yet developed universally validated strategies for developing theranostic clinical applications against Alzheimer's disease. However, given the emerging indications of the potentially enormous benefits that theranostics may bring to fight against AD, further rigorous research is warranted [6].

Liposomes and theranostics may have the future for fight against the Alzheimer's or neurodegenerative disorders in general. Transmembrane diffusion of drugs at blood brain barrier is usually permits only lipophilic drugs. Drugs for neurodegenerative disorders often find it difficult to transcend blood brain barrier. Flooding the bloodstream with drugs, where only a minor fraction reaches its target therapeutic site, is an inefficient, expensive, and dangerous procedure, because of the risk of side effects at nontargeted site [7]. Liposomes are vesicles or bags in which an aqueous volume is enclosed by a membrane made of lipid (fat), usually phospholipids. Liposomes can transport both lipophilic and hydrophilic drugs across blood brain barrier.

As a distinct feature of Alzheimer's disease (AD), the presence of excess metal ions in the brain is most probably one of the main causative factors for the aggregation of beta-amyloid proteins. Cui Z et al [8] designed a theranostic novel yet smart nanoprobe (UCHQ) for detection and control of ion  $\text{Cu}^{2+}$  concentration. Most importantly, UCHQs could not only inhibit the  $\text{A}\beta$  aggregation-induced apoptosis via capturing overmuch  $\text{Cu}^{2+}$  but also accelerate the nontoxic structural transformation of beta-amyloid [8]. Nanotechnology-based drug delivery system and Intranasal administration are promising. Intranasal drug delivery which offers an alternative, drug administration to the brain because drugs delivered this way can bypass the blood brain barrier and directly transport drugs to the central nervous system [1].

### Conclusions

This review summarizes the following: Beta-amyloid ( $\beta$ -A) peptides are very useful biomarkers for AD at the point-of-care (POC) level. Curcumin (CUR) effectively binds to beta-amyloid plaques and can cross blood brain barrier. Nanoimaging agent (NIA) recognizes and selectively binds to beta-amyloid plaques and is detected by MRI. Theranostics and liposomes contribute emerging indications required for fighting against AD effectively in the future. Nanoprobe inhibit the  $\text{A}\beta$  aggregation-induced apoptosis

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