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Alzheimer's Disease: The Role of Hyphenated Analytical Systems in the Analysis of Therapeutic Agents Effective against the Disease in Biological Fluids

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Editorial

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Editorial

Alzheimer's disease (AD) is a neurodegenerative disorder (brain disorder) that is irreversible, progressive and gradually destroys memory, thinking skills and ultimately the ability to carry out the minimal activities [1]. It is the most frequent type of dementia among elderly people. Dementia is characterized by the loss of cognitive functioning such as thinking, remembering, reasoning and behavioral abilities. Neuronal degeneration in Alzheimer's disease could be as a result of deposition of β-amyloid protein (Aβ) in the form of senile plaques, intraneuronal neurofibrillary tangles, protein tau(τ) hyperphosphorylation, oxidative stress and inflammation [2]. The neurochemical changes in Alzheimer's disease form the basis for the symptomatic treatment with drugs like donepezil, galantamine, memantine, rivastigmine and tacrine. They are used orally in the treatment of mild to moderate Alzheimer's disease. These drugs are competitive and reversible cholinesterase inhibitors (AChEI) inhibiting the activity of enzyme cholmesterase and increasing the level of acetylcholine in brain. A dysfunction of glutamatergic neurotransmission is also considered to be involved in the etiology of the disease. Memantine, an N-methyl D-aspartate antagonist (NMDA) acts on the glutamatergic system by blocking NMDA glutamate receptors and is utilized to treat moderate to severe form of the disease. Similarly, donepezil is the most widely used cholinesterase inhibitor probably due to its 100% bioavailability and ability to cross the blood-brain barrier.

A hyphenated technique is an on-line combination of a separation technique and one or more spectroscopic detection techniques [3]. It entails linking liquid chromatography (LC), usually a high-performance liquid chromatography (HPLC), gas chromatography (GC), or capillary electrophoresis (CE) to spectroscopic detection techniques such as photodiode array (PDA) UV-Vis absorbance, Fourier-transform infrared (FTIR), nuclear magnetic resonance (NMR), mass spectroscopy (MS). Due to the chronic nature and debilitating features of the disease, it has become very important to have a specific method for measuring these drugs in various biological matrices such as blood, serum, urine and cerebrospinal fluid etc. Determining them in long-term treatment enables drug doses to be adjusted, therapeutic effects to be ascertained and patient compliance to be ensured. Several methods reported for the determination of the clinically used cholinesterase inhibitors in biological matrices are mostlyhyphenated analytical systems. Non-hyphenated analytical methods are not frequently used because plasma volume requirement is high, sensitivity might be inadequate for pharmacokinetic studies, multiple sample preparation and extraction procedures are time-consuming.

Detection methods such as ultraviolet (UV), fluorescence have been used for donepezil, rivastigmine, galantamine, tacrine except memantine that lacks chromophore. However, derivatization procedures allow memantine to be detected by these detection methods. Mass spectrometry detection method has also been used for all cholinesterase inhibitors. Although, several methods have been reported for the assay of each of the cholinesterase inhibitors in biological fluids, only two to

three analytical methods shall be highlighted. Literature search has revealed that donepezil has been determined in human plasma by liquid chromatography/tandem mass spectrometry [4], high performance liquid chromatography with fluorescence detection [5]. Capillary zone electrophoretic technique [6] and high-performance liquid chromatography-tanden mass spectrometry (HPLC-MS/MS) [7] have been employed to determine galanthamine in biological fluids. The determination of rivastigmine, a relatively new drug used for the treatment of Alzheimer's disease has been done using flurometric method [8], HPLC [9], liquid chromatography-tandem mass spectrometry (LC–MS–MS) [10]. Furthermore, memantine has been determined by HPLC-MS-MS [11] and HPLC-MS [12] while tacrine has been determined by HPLC methods [13,14].

In conclusion, only few non-hyphenated analytical techniques have been used to determine clinically cholinesterase inhibitors for Alzheimer's disease. Amongst the hyphenated analytical methods, HPLC-MS/MS method has proven to be the analytical method of choice for the quantification of Alzheimer's disease drugs in both preclinical and clinical studies. This might be as a result of its specificity, accuracy, reproducibility, shortened analysis time, higher sample throughput, selectivity, high sensitivity and lower cost of analysis. Finally, hyphenated methods (in particular HPLC-MS/MS) have successfully been used to analyze therapeutic agents for Alzheimer's disease in human biological fluid samples for application in pharmacokinetic, bioavailability, or bioequivalence studies.

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