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Hungtington Disease: Biopharmaceutical Methods of Interest in the Quantification of Therapeutic Agents Utilized in the Management of the Disorder

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Editorial

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Editorial

Huntington's disease (Huntington chorea) is an autosomal inherited disorder of the central nervous system that is progressive [1]. It is characterized by extensive generative changes of the basal ganglia, cerebral cortex and other regions of the brain. The disease is caused by a single defective gene protein (huntingtin) on one of the 23 human chromosomes (chromosome 4) and the defect is "dominant" [2].

The symptoms of the disease can be categorized into [3]:

I. Physical symptoms: chorea- (involuntary movements of the limbs, face and body); continual muscular contractions; difficulty swallowing or eating; increased clumsiness; loss of coordination and balance; jaw clenching or teeth grinding; slurred speech; stumbling or falling.
II. Cognitive or mental symptoms: decreased concentration; difficulty making decisions or answering questions; forgetfulness and memory decline; loss of drive and initiative; poor judgment.
III. Emotional symptoms: anxiety; depression, irritability; obsessive-compulsive behavior; psychotic behavior's such as delusions, hallucination, unprovoked aggression and paranoia. Current clinical treatments are based on managing symptoms of the disease. For instance, drugs of choice for (a) chorea (involuntary movements) are olanzapine (atypical antipsychotic agent) and tetrabenazine (dopamine depleting agent),
IV. Irritability (severe anger and threatening behavior) are atypical antipsychotic drugs (clozapine, olanzapine) and selective serotonin reuptake inhibitors-antidepressants (fluoxetine, paroxetine, sertraline)
V. Obsessive-compulsive thoughts and actions are selective serotonin reuptake inhibitors (fluoxetine, sertraline).

In addition to these first-line drugs employed in the treatment of three of the disease's most troubling symptoms, other therapeutic agents such as benzodiazepines, glutamate antagonists are used in the management of other symptoms associated with the disorder.

Due to the complexity of the disease, various approaches involving different drugs and doses have been employed for effective treatment of symptoms. The effective treatment of symptoms can be achieved by administering these drugs as single dosage form containing two or more of the drugs or in their different dosage forms. Therefore, it requires accurate, precise, sensitive, selective and specific analytical methods in order to accurately quantify them in biological fluids. In the present article, attempt was made to examine analytical methods that have been used to determine in biological fluids these first -line drugs employed in the treatment of Huntington's disease. It is envisaged that

same analytical methods could be of use in their quantification when biological fluids of Huntington disease patients are analyzed.

Literature search has revealed that these first-line drugs have been determined in biological fluids using various analytical methods such spectroscopic and chromatographic methods.

However, chromatographic methods involving hyphenated or non-hyphenated systems are considered of interest since these drugs are administered mostly in combinations. The type of biological fluids and some of the analytical methods reported for these first-line drugs include:

I. Olanzapine, determined in: (a) whole blood Katrine M, et al. [4] by hyphenated system, (b) plasma Nirogi RV, et al. [5], Berna M, et al. [6] & Kollroser M, et al. [7] by Hyphenated system and Dusci LJ, et al. [8], Raggi MA, [9] & Raggi MA, et al. [10] by non-hyphenated system, (c) serum Berna M, et al. [6] & Harald W, et al. [11] by hyphenated and non-hyphenated system respectively (d) breast milk Kasper SC, et al. [12] by non-hyphenated system.

II. Tetrabenazine, determined in (a) plasma Derangula VR, et al. [13] by hyphenated system and Roberts M, et al. [14] by non-hyphenated system.

III. Clozapine, determined in (a) plasma Kollroser M, et al. [7], Song M, et al. [15] & Vardakou I, et al. [16] by hyphenated system (b) serum Harald W, et al. [11] & Zhou DW, et al. [17] by hyphenated system and non-hyphenated system respectively.

IV. Fluoxetine, determined in (a) plasma He J, et al. [18] by hyphenated system and Maya MT, et al. [19], Meineke I, et al. [20] & Jourdil NH, et al. [21] by non-hyphenated system (b) serum Lacassie E, et al. [22] by non-hyphenated system.

V. Paroxetine, determined in (a) plasma He J, et al. [18] by hyphenated system and Foglia JP, et al. [23], Shin JG, et al. [24] & Lopez-Calcull C, et al. [25] by non-hyphenated system (b) whole blood and urine Agrawal N, et al. [26] by non-hyphenated system.

VI. Sertraline, determined in (a) plasma Rogowsky D, et al. [27], Kim KM, [28] & Jain DS, et al. [29] by hyphenated system (b) serum Lacassie E, [30] by hyphenated system (c) breast milk Weisskopf E, et al. [31] by hyphenated system.

VII. The determination of the level of these drugs in the biological fluids of Huntington patients is very vital since one of the goals is to individualize patient therapy and dose selection (optimization of the dosage) to enhance the effect of the drug and minimize toxic effects. This is particularly important for these classes of drugs of which some may have narrow therapeutic index.

VIII. In conclusion, literature reports have shown that most of the analytical methods employed in the determination of first-line drugs in the management of Huntington's disease are hyphenated chromatographic methods. Although, these analytical methods are expensive, however, they not only successfully resolve these drugs from each other and also from the endogenous/exogenous plasma constituents but simultaneously identify them. Furthermore, their applications provide the reliability of quantitative assays for the determination of these drugs in biological fluids and the integrity of the resulting assay data. Finally, the results of the present study suggest that hyphenated or non-hyphenated chromatographic analytical methods are the analytical methods of interest to be used in quantification/identification of the first-line drugs utilized in the management of Huntington disease patients.

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