Preparation and molecular characterization of nanostructures of conjugated deferasirox to lactoferrin

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Background and Aims: Many neurodegenerative disorders including Parkinson's disease and Alzheimer's disease have been found to be associated with increased brain iron levels and chelation therapy is considered to be one of the important approaches in the management of these disorders. Lactoferrin, a protein from transferrin family which is significantly upregulated in the brain of patients affected by neurodegenerative diseases is a promising macromolecular vector for brain delivery of different potential drug molecules. Here in, the conjugation of an iron chelator agent, deferasirox, with lactoferrin have been used for the preparation of water soluble nano structured conjugates which may be used for drug delivery especially to brain tissues in neurodegenerative diseases.

An appropriate excess amount of deferasirox was dissolved in Dimethyl Sulfoxide (DMSO) and equivalent moles of N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (EDC) and N-hydroxy-3-sulfo-succinimide (SNHS) were added to this mixture and stirred overnight. A 50 µM lactoferrin solution in phosphate buffer 0.1 M plus 50 mM NaCl (pH= 7.3) was added to the mixture and was left to stir for one hour. The resulted conjugates were purified from the reagents mixture by extensive dialysis. The conjugation ratio was determined by a spectrophotometric method which monitored the amount of colorful complexes resulted from the complexation of deferasirox with Fe(II) at 515 nm. Lactoferrin concentrations were quantified by a modified Bradford method and the conjugation ratio was calculated. The conjugation ratio was determined to about 10 moles of deferasirox attached to each molecule of lactoferrin. The resulted nanostructures were analyzed with an Agilent gel permeation chromatography system and an elevation in the size and molecular weight of resulted conjugates was established. The nanostructures size was also determined by Malvern zeta sizer and The conjugates had an average size of 106 nm with a particle size distribution of 0.345.

Keywords: Deferasirox; Lactoferrin; Conjugation; Nanostructure