Abstract

Oxytocin (OT) is a peptide hormone and neurotransmitter involved in various biological functions through interacting with its cognate G protein-coupled receptors. In humans and other mammals, one oxytocin and three closely related vasopressin receptors such as V_{1a}, V_{1b}, and V_2. Oxytocin is a cyclic nonapeptide with a disulphide bond between Cys^1 and Cys^6. The biomedical use of oxytocin is limited by its short half-life *in vivo* and by the low receptor selectivity. However, the design and synthesis of OT-derived analogues can be interesting for imaging applications and targeting various diseases. The presented studies aim to increase the stability of oxytocin by replacing the disulphide bridge with the stable and more rigid 1*H*-[1,2,3]triazol-1-yl moiety. In this context, the Cu(I)-catalysed side chain-to-side chain azide-alkyne 1,3-cycloaddition (CuAAC) macrocyclisation strategy was employed to stabilise β-turns secondary structures. This doctoral dissertation reports the design, synthesis, conformational analysis, and *in vitro* pharmacological activity of a series of $C\alpha^1$-to-$C\alpha^6$ side chain-to-side chain 1*H*-[1,2,3]triazol-1-yl-containing oxytocin analogues differing in the length of the bridge and the orientation and location of the linking moieties. By developing this macrocyclisation method, it was possible to produce a series of compounds that provided attractive insight into the structure-conformation-function relationship.

Moreover, the secondary structure of peptides or proteins plays a crucial function in their bioactivity. In this sense, Myelin Basic Protein (MBP) peptides have been synthesised and played a significant role in effectively recognising IgM antibodies in Multiple Sclerosis (MuSc). MuSc is a demyelinating, neuroinflammatory, autoimmune disease that attacks the central nervous system (CNS). Genetic and environmental aspects, *e.g.*, viral and bacterial infections, participate in this process. The MBP is an intrinsically disordered protein demonstrating an interesting α-helix motif, which can be considered a conformational epitope. This PhD thesis investigated the role of the sequences and structures of synthetic MBP peptides that have been used to identify specific antibodies in Multiple Sclerosis patient sera. Therefore, the studies of the relationship between the secondary structure and the bioactivity of the series of MBP peptides are discussed.