

Peptide CART (cocaine- and amphetamine- regulated transcript) is a neuropeptide acting in the hypothalamus to reduce food intake (anorexigenic peptide). Despite all efforts the receptor and the mechanism of action is still unknown. This peptide has two biologically active forms, CART(55-102) and CART(61-102). Peptide CART is able to bind to pheochromocytoma cells PC12. PC12 cells differentiated in neuronal phenotype with NGF (nerve growth factor) showed a higher number of binding sites ( $11250 \pm 2520$  binding sites/cell) compared to undifferentiated cells ( $3600 \pm 570$  binding sites/cell). PC12 cells differentiated by dexamethasone to chromaffin cells showed high non-specific binding. Peptide CART contains three disulfide bridges. To clarify the importance of each disulfide bridge to maintain biological activity, analogues with one (analogue 3, 4 and 5) or two (2, 6, 7 and 8) disulfide bridges and a peptide analogue of CART (61-102), which has methionin at position 67 replaced with norleucine were synthesized. We showed that biological activity was unchanged at analogue 1 and analogue 7 containing disulfide bridges in positions 74-94 and 88-101. When investigating cell signaling in PC12 cells, we tested if peptide CART activate of c-Fos, c-Jun, phosphorylated ERK1/2, CREB, JNK and p38. CART peptide significantly increased activation of c-Jun, and non-significantly increased phosphorylation of JNK, which precedes c-Jun.