296/E2

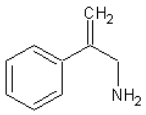
Study of interactions of a novel class of vesicular monoamine transporter inhibitors with bacterial cells to investigate the uptake mechanism

V N P Liyanage, R M L K Ratnayake, Rohan P Perera* and G H C M Hettiarachci,
Department of Chemistry, University of Colombo

It has been shown that many illicit drugs as well as some antidepressants and psychiatric drugs are good substrates for nerve cell monoamine transporter proteins in brain.

Recent studies show that 3-amino-2-phenylpropene (APP) (Fig.1(a)) and its derivatives are potent inhibitors for bovine vesicular monoamine transporter(s) and cytotoxic towards the SH-SY5Y nerve cells *in vitro*.

(a) (b)



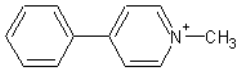


Fig 1: (a) 3-Amino-2-phenylpropene (APP) (b)1-Methyl-4-phenylpyridinium ion (MPP^+)

Recent experiments demonstrate that combination of APP with MPP^+ (Fig.1(b)) would produce inhibitors such as 4-phenyl-1-(2-phenyl-allyl)pyridinium bromide (APP-MPP^+, conjugated compound) (Fig. 2), which act as a potent inhibitor for bovine chromaffin granule vesicular monoamine transporter. It is believed that these compounds interact with transporter protein and change its conformation which allows compounds to interact with it. The mode of interaction and the mechanism of binding of these compounds to monoamine transporters are still not well understood. In this work *Escherichia coli, Bacillus, Staphylococcus aureus, Klebsiella* bacterial cells have been used as models to study interactions of APP-MPP^+ conjugate compounds with cells and to determine their cytotoxic effect. This investigation is focused on studying the interactions of APP-MPP^+ with microorganisms and their uptake mechanism.

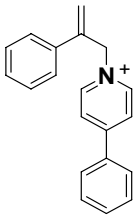


Fig 2: APP–MPP^+ Conjugated inhibitor, 4-phenyl-1-(2-phenyl-allyl)pyridinium bromide (APP-MPP^+)

These studies further indicate that this novel compound significantly inhibits the growth of *Escherichia coli* and it has minor effects on other bacterial cells too.

*rohan@chem.ac.lk Tel: 011 - 2503367