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

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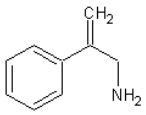
It has been shown that many illicit drugs as well as some antidepressants and psychiatric drugs are good substrates for nerve cell monoamine transporter proteins in brain.

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)



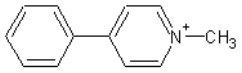


Fig 1: (a) 3-Amino-2-phenylpropene (APP) (b)1-Methyl-4-phenylpyridinium ion (MPP^+)

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.

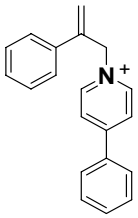


Fig 2: APP–MPP^+ Conjugated inhibitor, 4-phenyl-1-(2-phenyl-allyl)pyridinium bromide (APP-MPP^+)

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.

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Quality of water consumed by chronic kidney patients in North Central province of Sri Lanka

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The population of the North Central Province (NCP) is about 1.2 million and geographically it is the largest province in the country. Majority of rural population living in the area are farmers and they largely depend on the ground and surface water sources for their day to day life. At present, over 5,000 patients in NCP are on treatment for Chronic Kidney Diseases (CKD) and the etiology for this disease still remains a mystery.

'Heavy metals' are chemical elements with a specific gravity that is at least 5 times the specific gravity of water. Living organisms require trace amounts of some essential metals but excessive levels can be detrimental to the organisms. Toxic metals have no known vital or beneficial effect on organisms, and their accumulation over a period of time in human bodies can cause serious illnesses like CKD. In addition, some potential triggering factors for CKD are PO_4^{3-}, SO_4^{2-}, F^- and Mg.

According to the surveys done in Anuradhapura and Madawachchiya renal clinics, two affected areas Wewalkatiya and Nikiniyawa villages in Anuradhapura district and a reference village, Kohalwila, where no CKD patients were found were selected for water quality testing. The water distribution reservoir in Kekirawa affected area, Malawa tank, was selected as the surface water source. Sampling was done from ground water wells in patient houses, Malawa tank and reference village in dry and wet seasons by collecting 3 samples at a point totally 20 points from a site. The concentrations of Fe, Al, Zn, Cu, Cd, Cr, Ca, Mg, Ni, Mn and Pb were determined by Atomic Absorption Spectrophotometry (AAS). The concentrations of total phosphorous, available phosphate, available sulphate and fluoride were determined by standard methods, pH was measured and total soluble ions were determined by conductivity measurements.

The mean concentration of the analyzed metals in water samples from Anuradhapura district show very higher values than the reference site. Dissolved metal concentrations in analyzed water samples in affected areas do not exceed the Maximum Contaminated Levels set by the WHO for drinking water except for Al, Mn and Ni. The triggering factors of CKD, Mg, P, SO_4^{2-}, PO_4^{3-} and F^- accumulated in water in the affected area are very high compared to the reference site. Although these concentrations reduce in wet season, these values are always higher than the values obtained for the reference site.

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