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Interaction of serotonin and melatonin with sodium, potassium, calcium, lithium and aluminium

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Abstract: In the present study, we investigated the ability of serotonin and melatonin to bind metals that occur naturally in the brain. An electrochemical technique called adsorptive cathodic stripping voltammetry (AdCSV) was employed to study the metal–serotonin or metal–melatonin interactions. The results show that both serotonin and melatonin form stable complexes with lithium and potassium, with serotonin favouring lithium over potassium, and melatonin favouring potassium over lithium. Coordination between either serotonin or melatonin and calcium was not favoured. The stability of the complexes formed between serotonin and the metals decreased with the metals as follows: $Li^+ > K^+ > Al^{3+} > Na^+ > Ca^{2+}$. The trend for melatonin–metal complexes was $K^+ > Li^+ > Na^+ > Al^{3+} > Ca^{2+}$. The binding and stable complex formation between both ligands, serotonin and melatonin with lithium, potassium and sodium is of biological importance. The binding of serotonin to lithium could provide an explanation for the therapeutic effects of lithium in depression treatment, whereas the binding of aluminium by melatonin could provide insight into the role of this element in the aetiology of Alzheimer's disease.

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Introduction

The electrochemistry of serotonin, melatonin and tryptophan in the absence of metals has been described by Zoulis et al. [1990] and Radi and Bekhiet [1998] using stripping voltammetry methods. Recently, Limson et al. [1998] demonstrated the interaction of melatonin, and its precursors, with cadmium, copper, iron, lead, zinc and aluminium dissolved in acetonitrile using adsorptive cathodic stripping voltammetry (AdCSV).

Melatonin, and its precursor serotonin, have been shown to interact with a number of metal ions either by altering their actions or by altering their conductance through biological membranes. Such interactions have been shown to have possible biological significance, particularly with reference to melatonin's ability to protect against tissue damage [Daya, 1999]. Melatonin is known to stimulate voltage-dependent, sodium-selective currents and also stimulate tetrodotoxin insensitive voltage-dependent sodium current by a novel mechanism [Rich et al., 1999]. Potassium ion channels and guanylyl cyclases have also been reported to be modulated by melatonin [Petit et al., 1998]. Melatonin has been shown to play a role in regulation of potassium, sodium and chloride in the common dentex, *Dentex dentex* [Pavlidis et al., 1999]. The hormone also inhibits the activity of large conductance calcium-activated potassium channels [Geary et al., 1998], suggesting that melatonin inhibits endothelial potassium channels to decrease flow-induced release of nitric oxide and blocks smooth muscle potassium channels to enhance vascular tone. Melatonin has also been shown to interact with lithium [Lauber and Vriend, 1989] and aluminium [Limson et al., 1998]. The actions of serotonin have been noted to modulate both calcium [Hirafuji et al., 1999] and potassium currents [Herness and Chen, 2000].

In the present study, we describe the interaction of melatonin and serotonin with sodium, potassium, calcium, lithium and aluminium in aqueous media and under biological pH conditions. The study was conducted using a stripping voltammetry technique, the AdCSV method [Wang, 1989; Zoulis et al., 1990; Wang et al., 1993; Zhang et al.,