E2-32: Interaction of metal ions with some drugs

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Metal ions are an integral part of biological systems. Some trace metals are essential components of biologically important molecules such as haeme proteins and metalloenzymes. The importance of metal chelates is also recognised in medicinal chemistry. Metal chelates are used for medical purposes; excess metal ions can be removed from the system in the form of a stable chelated complex. It is also believed that chelation of metal ions by drugs facilitates drugs-receptor interactions. Another aspect of chelation is where formation of a drug-metal ion complex is actually undesirable.

This study investigates complex formation in the adrenergic drugs Salbutamol and Propranolol with a variety of metal ions (Fe^{3+}, Zn^{2+}, Cu^{2+}, Ni^{2+}, Cd^{2+}, Mg^{2+} and Ca^{2+}). UV/Vis spectroscopic, potentiometric and polarographic techniques were employed.

The UV spectra of Salbutamol and Propranolol were characterized by an absorption maximum at 301 nm and 294 nm respectively (pH 7). In the presence of a metal ion the intensity of absorption was enhanced, indicating complex formation. A more detailed study with Fe^{3+}, shows this increase to be linear over a wide range, with increasing Fe^{3+} concentration.

Further evidence for complexation was obtained from potentiometric studies. The potentiometric curve of the drug was displaced in the presence of metal ions. Based on this, a qualitative estimation of the stability of the Metal ion-Drug complexes was made.

With propranolol $Cd^{2+} > Cu^{2+} > Zn^{2+} \sim Fe^{3+} \geq Ca^{2+}$

With salbutamol $Zn^{2+} \sim Cd^{2+} > Ni^{2+} \sim Cu^{2+} > Ca^{2+}$

A polarographic study was also carried out, to obtain a quantitative measure of the stability of the metal ion-drug complexes formed. Cu^{2+} with a characteristic E½ value was the metal ion of choice. This potential was found to vary significantly in the presence of salbutamol and propranolol, confirming complex formation. Comparison of the potentials clearly shows the Cu^{2+} complex of propranolol to be more stable than that of salbutamol.