CHAPTER 1

INTRODUCTION

Chemistry of Schiff bases has been intensively investigated in recent years, owing to their coordination properties and diverse biological applications. Schiff base hydrazones are widely used in analytical chemistry as a selective metal extracting agent as well as in spectroscopic determination of certain transition metals. Since the beginning of medicinal chemistry, scientists had put efforts to find the relationship between chemical structures and biological activities. This can be proven with the invention of derivatives from steroid and antibiotic which had led to the discoveries of anti-inflammatory, anti-bacterial and antiviral agents. The invention is particularly advantageous in its targets as to specify substituent of molecules which have been proven playing a prominent role in reducing side effects and toxicity profiles (J. Costamagna *et al.,* 1992).

Schiff bases are compounds which contain an azomethine group (C=N) and are usually formed by the condensation of a primary amine with an active carbonyl compounds (aldehydes or ketones). Interaction of metal ions with N, O and S contain organic moieties have attracted much attention in recent years. This interaction provides an interesting series of ligands whose properties can be greatly modified by introducing different organic substituents, thereby causing a variation in the ultimate donor properties. This Schiff base complexes have different geometries and properties. Schiff bases were also found to be biologically active and show excellent biological properties such as anti-oxidant, anti-viral, anti-bacterial, anti-fungal and many other properties (S. N. Pandeya *et al*., 1999).

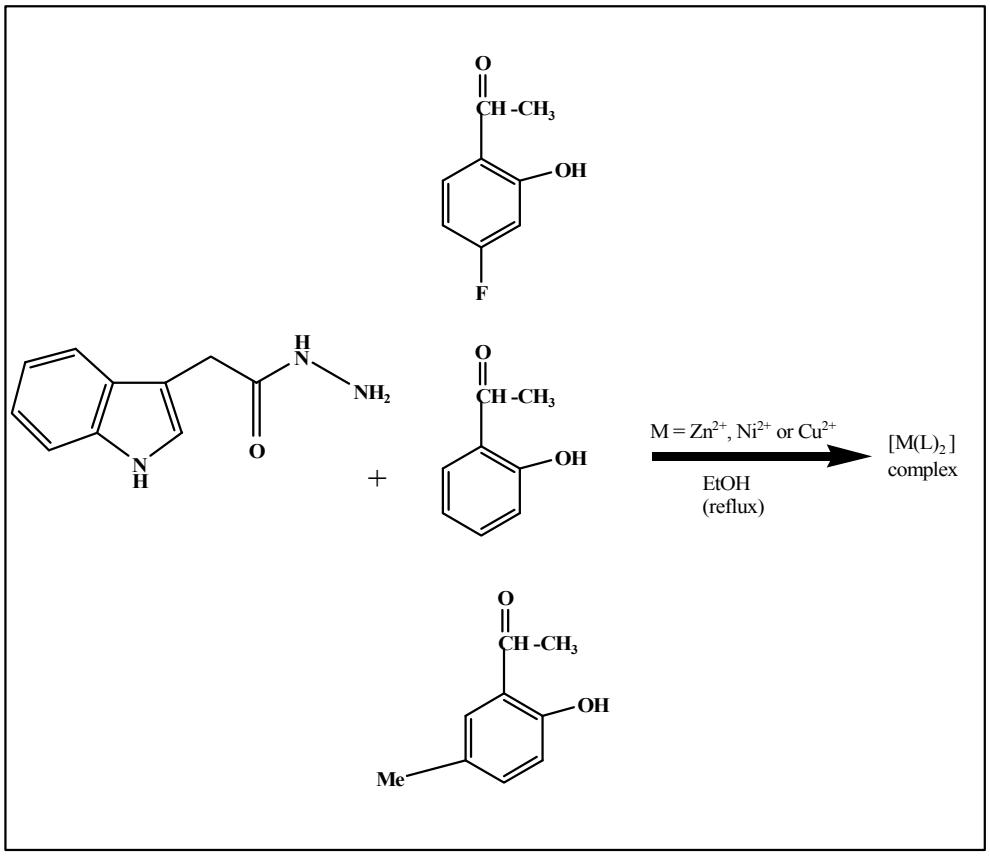
Recently, reactions of transition metal ion with hydrazones and their derivatives have attracted increasing attention over the past few decades. Many complexes derived from hydrazones such as thiosemicarbazones, have been reported (A. L Gerber, *et al* ., 1992). Compounds of hydrazones have a great biological activity such as anti-mural, anti-bacterial, anti-viral, anti –malaria and anti-tuberculosis effects (J. Costamagna *et al*., 1992).

However, it is still a challenge to bioinorganic chemists to deepen the investigation on the relationship between structures and biological activities. The study of the nitrogen, oxygen and sulfur donor ligands continue to be of great interest since the properties of these ligands can be modified through organic substituents.

Previous studies on indole hydrazone Schiff bases and their metal complexes were first reported in 1986, where the complexes of Cu (II), Ni (II) and Co (II) were characterized by mass spectra, IR, H-NMR, UV-Visible spectra and magnetic measurements (M. A. Hapipah, *et al*., 2003). However, there is no biological properties reported on indoles or indole hydrazones derivatives as well as their metal complexes.

Thus, the present study involves synthesis of indole-hydrazones derived from indole-3-acetic acid hydrazide and hydroxyacetophenone derivatives (Scheme 1) and their zinc(II), nickel (II) and copper(II) complexes. The Schiff bases and their metal complexes were characterized by various physico-chemical techniques including elemental analysis, IR, ^{1}H and ^{13}C NMR, UV- visible, TGA and single-crystal x-ray

diffraction. The electrochemical behaviour of the ligands and their metal complexes were investigated by using cyclic voltammetry technique. This technique was used to study the redox properties of the compounds. The Schiff bases and their metal complexes were also screened for anti-ulcerogenic activity to examine the protective effect of the compounds against ethanol-induced gastric lesions in Sprague-Dawley rats.



Scheme 1

The objective part of this research was on to synthesize and characterize ligands and metal complexes of indole hydrazones and its derivatives. Initially, indole hydrazone have also revealed very versatile behavior in coordination to metal as well as diverse biological and anti-ulcerogenic activities to be applied as new drugs for anti-ulcer.