CHAPTER I

Introduction

1.1 Introduction

Ideally, renal function should be evaluated with a single radiopharmaceutical that possesses high extraction efficiency[1,2], such as ^{131}I-OIH (Iodine-131 ortho-Iodohippuric acid). This agent should be labelled with radionuclide having good physical properties such as ^{99m}Tc (Technetium-99m). Currently ^{131}I-OIH and ^{99m}Tc-DTPA agents are commonly used in the evaluation of renal function.

Renal perfusion is performed by rapid serial imaging during the first circulation after bolus injection of ^{99m}Tc-DTPA. The ^{131}I-OIH can not be used for this purpose because the iodine-131 labelled compound limits the spatial resolution in the resulting images. Renal clearance can be determined by either ^{99m}Tc-DTPA or ^{131}I-OIH. Since ^{99m}Tc-DTPA is limited to clearance by glomerular filtration, the maximum extraction efficiency is only 20%. In addition to glomerlular filltration, ^{131}I-OIH is secreted by renal tubula, resulting in extraction efficiency of 67%. The higher extraction efficiency of ^{131}I-OIH increases the kidney-to-background image ratio , thus increases the sensitivity of ^{131}I-OIH for detection and evaluation of reduced renal function.

According to the radiation safety,many technetium-99m complexes have been synthesized and studied for potential replacements for ^{131}I-OIH. In 1986 many types of ligand were studied by Fritzberg[1,2]. A novel ligand corresponding to this consideration, MAG_3 (mercaptoacetyl glycylglycylglycine) was synthesized. The synthesized MAG_3 could form complex with technetium-99m and it has been evaluated as a good renal imaging agent [3]. This complex was ^{99m}Tc-MAG_3 ([(N-(N-(N-(mercaptoacetyl) glycyl) glycyl) glycinato(2-)N,N',N" ,S) oxotechnetate (2-)])[4].

The evaluation process for any drug or substance for human use includes test for safety and efficiency. As far as the user is concerned, the most important specifications are the quality control of the end-product and clinical assessment.[5].

The Tc^{99m}-MAG_3 complex has been standardized by the quality control programme established by Bureau of Oncology and Radiopharmaceutical of the US FDA Rockville, Maryland. The ^{99m}Tc-MAG_3 complex can be disturbed by small amounts of some metal ions. However, this study is not comprise in the quality control programme. There were some previous studies of the effect of metal on ^{99m}Tc complex ; the metal ions such as Sn^{4+}, Sn^{2+}, and Ca^{2+} which are contaminations in radiopharmaceutical [6-9]. The ^{99m}Tc-MAG_3 should be, therefore, affected by the metal ions in human body.

The adult human body contains 100-150 mg of copper. About 64 mg of which are found in the muscles, 23 mg in the bones, and 18 mg in the liver. These three organs contain higher concentration of copper than any other organs. It is of interest that the concentration of copper in the fetal liver is 5-10 times higher than that in the liver of an adult. Both the blood cells and serum contain copper. The copper content in the red blood cell is constant, while that in the serum is highly variable, averaging about 90 µg/dl [10-11].

The effect of copper ion on the ^{99m}Tc-MAG_3 complex might occur either by ligand exchange reaction or binding of Cu(II) with ^{99m}Tc-MAG_3. In order to study the influence of copper ion on ^{99m}Tc-MAG_3, the complex formation constant and the species distribution of copper with MAG_3 have been determined.

1.2 Objectives of the Research

The main purpose of this research is to study the influence of copper ion, (Cu(II)), on the ^{99m}Tc-MAG_3 complex. Firstly, the MAG_3 ligand will be studied by potentiometric titration. Secondly, the stability constants of the Cu(II) ion with MAG_3 will be determined by computer refinement using the potentiometric data. The complex formation will be also studies by UV/vis spectroscopic method in order to confirm the

potentiometric result. The radiochemical purity of ^{99m}Tc-MAG_3 complex in the presence of various concentrations of Cu(II) ion will be observed by paper chromatographic method. Since the S-benzoyl-MAG_3 ligand is not available from the commercial supplier so far, it is necessary to synthesize the compound. Development of a reliable method will be attempted for formulation of the MAG_3 kit which is suitable for labelling with ^{99m}Tc.