CHAPTER I

INTRODUCTION

Since the discovery of X-ray in 1895 by Roentgen and natural radioactivity in 1896 by Becquerel, the utilization of radiation in medicine has been developed. For the last decade, there has been a remarkable increase in varieties of clinical nuclear medicine studies. Due to the rapid advance in instrumentation, which is faster than radiopharmaceutical development, the study of every organ system has been materially affected by the development of highly specific radiopharmaceuticals. Generally, the new formulations should provide more clinical information at a lower radiation burden than their earlier analogues.

Early nuclear medicine studies of renal function were performed with radiolabeled contrast agent, usually with ^{131}I. These radiopharmaceuticals were unsatisfactory for renal studies because excretion of these agents often were not specific to the kidneys, resulting in poor resolution and higher dose of radioactivity must be used. For these reasons the radiopharmaceuticals that are excreted predominantly by the kidneys has been developed. Radioactive substances excreted either by glomerular filtration or tubular secretion is useful in evaluating renal function while radiopharmaceuticals either slowly excretes or bound within the renal cortex are useful for imaging renal anatomy (Chilton and Witcofski,1986).

Technetium Tc 99m Succimer Injection, which is commonly known as Technetium Tc 99m Dimercaptosuccinic acid or **^{99m}Tc-DMSA**, is one of the radiopharmaceutical agents useful for renal cortex visualization. It was first introduced by Lin, Khentigan and Winchell (Lin, Khentigan and Winchell,1974) as a technetium chelate substitute for radiomercurial (^{203}Hg) renal agents. An advantage of this compound over the other is the decrease of high absorbed radiation dose in vivo (Blaufox, Chervu and Freeman,1975). Technetium Tc 99m Succimer Injection is official in USP XXII as a sterile, clear, colorless solution of succimer complexed with technetium 99m. It contains not less than 85.0 % of the labeled amount of technetium Tc 99m as the succimer complex expressed in megabecquerels (microcuries or millicuries) per ml. It is recommended as a compound of choice for static renal scanning, especially in the assessment and serial follow-up of patients with disease that are liable to destroy the cortex progressively (Sutton, 1987; De Lange et al.,1989; Mackenzie, 1990).

Basically, Technetium Tc 99m succimer complex is formed when sodium pertechnetate Tc 99m is mixed with a solution of stannous chloride and dimercaptosuccinic acid. Nowadays, many brands of **Ready-To-Use kits**, or **Cold Kits** are commercially available. The kits contain dimercaptosuccinic acid and other non-radioactive additives. On the day of use the technetium Tc 99m is added under optimum condition, the Technetium Tc 99m succimer complex is formed.

In Thailand, two types of commercial succimer cold kits, imported and local made, are available. The local made kit has advantages on price and delivery time. However, it is not popular among users. From the data surveyed in one of the

government hospital in Bangkok during October 1991 to April 1992 (private communication), the locally produced kit usually yields unclear image whereas the imported kit does not. Generally, unexpected patterns of radiopharmaceutical biodistribution, which generates a flurry of examination, are affected by the quality of the administered agent. This unexpected biodistribution might be related to non radiopharmaceutical factors. In most case the improperly formulated radiopharmaceutical might be the cause. As a matter of fact, there are many possible factors that can affect the quality of technetium labeled radiopharmaceutical, for examples, radiolytic decomposition, pH ,ligand concentration (Ikeda et al.,1977; Krejcarek et al.,1976), and also factor caused by personnel.

Objectives

1. To study the technique for formulation of Technetium Tc 99m Succimer injection by means of the non radioactive constituents used for radiolabeling purpose.

2. To study the properties of the resulting formulations such as radiolabeling properties, stability of the labeled product and in vivo biological properties of the labeled product.

3. To determine the need of in house quality control for the labeled preparation, which should be performed before use for diagnosis.

The significance of the study

1. This study will provide the information concerning with the formulation of Technetium Tc 99m Succimer injection. This information can be used as a guideline for formulation, as well as evaluation, of the radiopharmaceuticals produced in Thailand to increase the reliability of the local produced radiopharmaceuticals. The result will be useful for promotion of local produced kit rather than the expensive imported products, which lead to the reduction of the service cost in the future.

2. The information concerning with the stability of Technetium Tc99m Succimer Injection will be helpful for determination of the need of in house quality control,which is supposed to be done prior to injection. Practically each vial of cold kit for single labeling is used as a multiple dose for more than one patient. This radiopharmaceutical requires thirty minutes scan time to complete the gamma scintigraphy. Further more, the drug is often administered after labeling for many hours due to the limitation of equipment as well as the course of service. This study will be determined whether the post labeling time affects the result or not.