CHAPTER I
INTRODUCTION

I.1. Background

Recently, pharmaceutical industries have developed more than 40% NCE (New Chemical Entities) to satisfy the needs of rapid treatment toward various diseases [1]. Nevertheless, majority of those developments have several problems for instance low solubility and/or low permeability therefore require a suitable system to be applied. Drug delivery is one of the common approach to resolve several problems involving pharmaceutical compounds where the compound is transported safely to a designated target in the human body using specific drug carrier [2]. Several drug carriers have been developed within the past years, yet most of it possess a low loading capacity and limited structural adjustment.

Metal-Organic Framework (MOF) is a particle composed of metals and organic ligands with a high surface area and adjustable porosity. The use of this material as a drug carrier has been widely developed yet the opportunity still extensive, predominantly the MIL family [3]. MIL-100(Fe) is a Metal-Organic Framework comprises Fe(II) or Fe(III) as the metal connector and H_3BTC as the ligand linker. Transition metals such as Fe(II) and Fe(III) found to be important for biological processes in the body [4], while H_3BTC toxicity has been tested to the body and found to be biocompatible [5]. The preparation of MIL-100(Fe) in this study is conducted at room temperature by substituting the hazardous chemicals (i.e., HF and HNO_3) with NaOH [6].

Furosemide is a loop diuretic drug used to treat hypertension and relieve swelling caused by heart failure, liver disease, and kidney disease. Furosemide has a low solubility in aqueous solution ranging from 0.18 mg mL^{-1} at pH 2.3 to 13.36 mg mL^{-1} at pH 10 [7]. Several techniques have been carried out to either increase the solubility or optimize the delivery system of Furosemide, such as using co-solvents [8], pH control [9], nano-encapsulation [10], solid dispersion [11], complexation with cyclodextrin [12], microcrystalline cellulose [13], and composite hydrogels [14]. Nevertheless, most of the results are yet unsatisfying thus require further exploration.

To the best of our knowledge, the delivery of Furosemide utilizing tunable particle such as MIL-100(Fe) has yet been studied, predominantly MIL-100(Fe) synthesized via safer route since the conventional method to synthesize MIL-100(Fe) requires highly thermal conditions and hazardous chemicals which is harmful. Furthermore, the influence of NaOH on the formation of MIL-100(Fe) has yet to be found despite the fact that NaOH played an essential role in the synthesis process. Hence in this research, the drug delivery of Furosemide using MIL-100(Fe) synthesize via safer route and influence of NaOH toward the formation of MIL-100(Fe) will be studied. Moreover, various mathematical model regarding the loading and release of Furosemide will also be studied to comprehend its behavior.

I.2. Objectives

- To study the effect of NaOH on the synthesis of Metal-Organic Framework (MOF) via non-solvothermal method under stirring condition.
- To study the effect of adsorbent dose on the loading of Furosemide into MOF as Drug Carrier.
- To determine the adsorption kinetic and isotherm of Furosemide into Metal-Organic Framework.
- To study the release of Furosemide from MOF.
- To determine the release kinetic of Furosemide from Metal-Organic Framework.

I.3. Scopes of Research

- Metal-Organic Framework (MOF) was synthesized by stirring a mixture of Fe, BTC, NaOH, and H_2O (also known as MIL-100(Fe)) with varying proportions at room temperature for 24 h, where molar ratios of Fe: BTC: NaOH: H_2O used is 1.5: 1: X: 880 with X ranging from 1.5 to 5.0 [6].
- Effect of adsorbent dose on the loading of Furosemide into MOF was investigated by varying the masses of adsorbent in a constant solvent volume, where the mass of MOF used ranging from 10 to 30 mg with intervals of 10 mg.
- Release of Furosemide from MOF was investigated at multiple values of pH to imitate different parts of

gastrointestinal tract, which are phosphate buffer solution (PBS) pH 5.8 and 7.4 [14].