# UNIVERSITI TEKNOLOGI MARA

# A STUDY ON NUCLEATION KINETICS OF CARBAMAZEPINE-FUMARIC ACID FORM B COCRYSTAL

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# ABSTRACT

Cocrystallization is a common technique selected by many researchers in purpose to enhance pharmaceutical drugs properties and nucleation kinetics is one of the important parameter to perform cocrystallization. However, the nucleation kinetics for carbamazepine-fumaric acid form B cocrystal has not been studied. The purpose of this experiment is to study on nucleation kinetics of CBZ-FUM acid form B by using Nývlt's approach. In this study, carbamazepine (CBZ) was selected as API and fumaric acid (FUM) was used as coformer in order to produce CBZ-FUM form B cocrystal. To ensure form B was produced, stoichiometric ratio of 1:2 of CBZ to FUM was used in this study. Metastable zone width (MSZW) was studied by manipulating the solution concentration in range from 0.0467 g/mL to 0.0512 g/mL. Besides that, the effect of cooling rate on MSZW also was studied by varying the cooling rate (0.10, 0.25, 0.50, and 0.75 ˚C/min). Based on results obtained, the MSZW was increased as cooling rate increases but concentration has insignificant effect on MSZW. The nucleation rate obtained was in range of 0.1325 to 1.3052. Cocrystal also undergoes characterization process by using FTIR microscopy and optical microscope. Based on FTIR results, cocrystal peaks was formed at above and below of pure component peaks. For XRPD result, it shows that CBZ-FUM form B cocrystal has developed 5 new peaks in between 6.6˚ and 34˚ 2θ. Meanwhile, peaks on DSC result between range 185 ˚C and 186.5 ˚C were proved the formation of form B polymorph. Lastly, CBZ-FUM form B cocrystal that formed has needle-liked morphology.

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# CHAPTER ONE
# INTRODUCTION

## 1.1 BACKGROUND OF STUDY

Pharmaceutical drug is use for the purpose of preventing, curing and treating different types of diseases and illness. In pharmaceutical industry, these drugs are called as medicines. This pharmaceutical drug is able to relieve pain and help to control the severity of mental and physical diseases. Examples of diseases and illness that can be treat or control by using pharmaceutical drugs is cough and cold, diabetes, cancer, headache, heart attack, hypertension, epilepsy, and many other diseases.

Carbamazepine is one of the examples of pharmaceutical drug or medicine. Carbamazepine is an anticonvulsant used to treat seizures and nerve pain such as diabetic neuropathy and bipolar disorder. Anticonvulsant is a drug substance that prevents or reduces the severity and seizure frequency of epilepsy disease. This anticonvulsant has different mode of action when it acts on different receptors in the brain.

Pharmaceutical drug is classified into several classes based on its pharmaceutical properties. For example, carbamazepine is classified as a class III pharmaceutical agent. This type of class has unique and different characteristic compared to other classes. Class III product has low solubility but high permeability in the biopharmaceutical system (Limwikrant *et al*, 2012).

Poor solubility of pharmaceutical product is a common problem faced by pharmaceutical manufacturers during handling this drug. Drugs that have poor solubility properties will lead to slow dissolution in biological system, insufficient and lack of efficiency of the drug performance (Rahim *et al*, 2015). Besides that, solubility of drug is a main key for pharmaceutical drug performance. According to Rahim *at el*, low biosorption properties, toxicity and lack of efficacy are the major reason of only less than 1% of active pharmaceutical ingredient is produce into the market place.