Cocrystal physical stability test was carried out to determine the effect of temperature and humidity on the physical stability of quercetin-isonicotinamide cocrystal. The results of cocrystal physical stability test for 7 days showed that cocrystal with 1: 3 ratio had better stability under the influence of temperature and humidity, compared to cocrystal with a ratio of 1: 1. This shows that the difference in the ratio can affect the stability of the resulting cocrystal.

This research has proven that quercetin-isonicotinamide cocrystal can form supramolecular heterosynthon through hydrogen bonds interaction. Quercetin-isonicotinamide cocrystal shows increased in its solubility and dissolution rate, as well as differences in the physico-chemical characteristics. The difference in the ratio between quercetin and isonicotinamide will affect the physico-chemical characteristics, solubility, dissolution, and physical stability of quercetin –isonicotinamide cocrystal.

# ABSTRACT

## Quercetin Crystal Engineering – Preparation of Quercetin-Isonicotinamide Cocrystal to Improve Solubility and Disolution Rate

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Development of drug ingredients derived from natural materials is a potential way to produce active pharmaceutical ingredients with less side effects. Active pharmaceutical ingredients derived from natural ingredients are expected to provide potent effectiveness such as synthetic compounds. This dissertation will researching quercetin as one of the potential bioactive compounds to be developed as a candidate for active pharmaceutical ingredients. Quercetin is one of the many flavonoid compounds found in various plants. Various pharmacological activities of quercetin show the potential of quercetin to be developed into active pharmaceutical ingredients. The challenge in developing quercetin as an active pharmaceutical ingredient is its poorly water solubility (0.01 mg / mL at 25°C). This low water solubility will cause a low dissolution rate of quercetin in the body, so the amount of dissolved quercetin that can be absorbed by the body will also be low.

This research aim is to develop quercetin cocrystal products to improve the physicochemical characteristics of quercetin in the aspects of solubility and the rate of dissolution, as well as the observation of the physical stability of the resulting cocrystal.

Molecular modelling were used to determine the coformer in cocrystal preparations. Binary phase system was made to determine the cocrystal ratio to be used. Cocrystal characterization was performed by thermal analysis (DSC), crystallinity (PXRD), crystal surface morphology (SEM), and infrared spectroscopic analysis (FTIR). Determination of the solubility and dissolution characteristics was carried out using a buffer solution of pH 5.0, while a physical stability study of quercetin cocrystal was also carried out.

The selected coformer is a coformer that can form hydrogen bonds with quercetin with the smalles minimize energy, namely isonikotinamida (20,0103 kcal / mol). Cocrystal was prepared in three different stoichiometric ratio of quercetin-isonicotinamide. Quercetin-isonicotinamide cocrystal preparation was carried out by the solvent evaporation method, using ethanol as a solvent. The solubility test results show that quercetin-isonicotinamide cocrystal with a ratio of 1:1 and 1:3 has a higher solubility when compared to the solubility of quercetin, whereas cocrystal with a ratio of 3: 2 does not show an increase in solubility. The dissolution test results showed a correlation with the results of the solubility test and cocrystal characterization tests which included thermal analysis, crystallinity, crystal surface morphology, and vibrational transition analysis. Cocrystal with a ratio of 1: 3 shows the highest value of dissolution rate which is 97.68% in the dissolution test for 6 hours. The results of cocrystal physical stability test for 7 days showed that cocrystal with 1: 3 ratio had better stability under the influence of temperature and humidity,

This research has proven that quercetin-isonicotinamide cocrystal can form supramolecular heterosynthon through hydrogen bonds interaction. Quercetin-isonicotinamide cocrystal shows increased in its solubility and dissolution rate, as well as differences in the physico-chemical characteristics. The difference in the ratio between quercetin and isonicotinamide will affect the physico-chemical characteristics, solubility, dissolution, and physical stability of quercetin –isonicotinamide cocrystal.