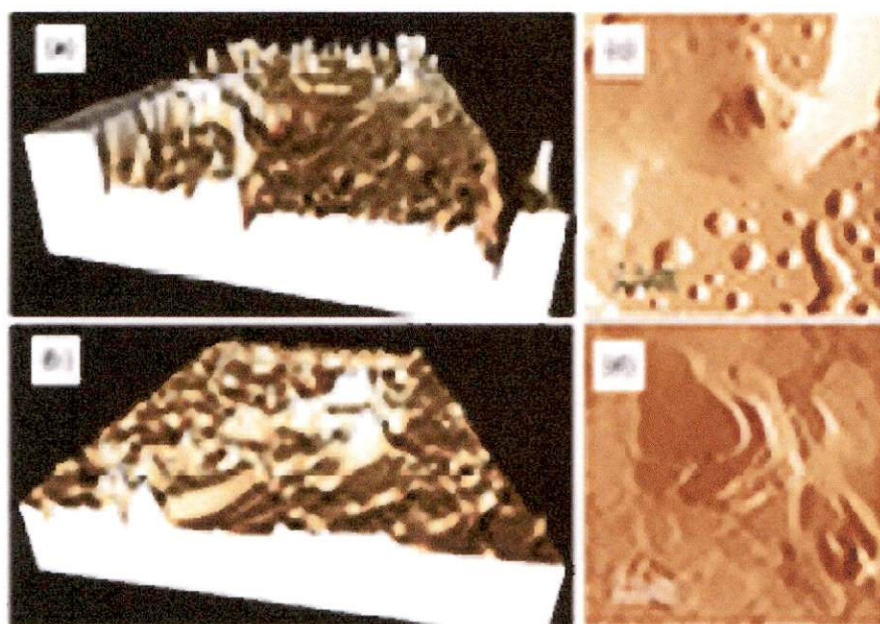


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Fig. 1. Fig. 2. Fig. 3. Fig. 4.



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Improvement *in vitro* Dissolution Rate of Quercetin Using Cocrystallization of Quercetin-Malonic Acid

Dwi Setyawan*, Sukma Adhi Permata, Ahmad Zainul, and Maria Lucia Ardhani Dwi Lestari

Department of Pharmaceutics, Faculty of Pharmacy, Universitas Airlangga,
Jl. Dharmawangsa Dalam, Surabaya 60286, Indonesia

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ABSTRACT

The aim of the study was to improve the *in-vitro* dissolution rate of quercetin (Qu) using cocrystallization of quercetin. Cocrystals of quercetin (Co Qu) were produced with malonic acid (Ma) as coformer at ratio 1:2 using solvent evaporation method. Cocrystals quercetin-malonic acid (Co Qu-Ma) was characterized using Differential Thermal Analysis (DTA), Powder X-Ray Diffraction (PXRD), Scanning Electron Microscope (SEM), and Fourier Transforms Infrared Spectrophotometer (FTIR) and *in-vitro* dissolution study. A new endothermic peak at 277.9 °C was shown from the thermogram. Diffractogram of Co Qu-Ma showed a new diffraction peak at 2θ 9.81, 12.99, and 19.80°. Microphotograph showed that Qu and Ma exhibited a columnar-shaped and a pebble-shaped crystal, respectively, and FTIR wavenumber of O-H functional group of quercetin was shifted from its original position at 3411 to 3428 cm^{-1} in the physical mixture (pm) of Qu-Ma and 3418 cm^{-1} in Co Qu-Ma, respectively. The physicochemical characterizations using DTA, PXRD, SEM and FTIR indicated that Co Qu-Ma were successfully obtained through solvent evaporation method. The *in-vitro* dissolution rate of Co Qu-Ma was 95.30% at 60 min. Cocrystals effectively increased dissolution rate and dissolution efficiency in comparison to the pure quercetin and physical mixture of quercetin-malonic acid.

Keywords: quercetin; malonic acid; cocrystal; *in-vitro* dissolution

ABSTRAK

Penelitian ini bertujuan untuk meningkatkan laju disolusi kuersetin (Qu) secara *in-vitro* melalui metode kokristalisasi kuersetin. Kokristal kuersetin (Co Qu) dibuat menggunakan metode evaporasi pelarut dengan koformer berupa asam malonat (Ma) pada perbandingan 1:2. Kokristal kuersetin-asam malonat (Co Qu-Ma) yang dihasilkan kemudian dikarakterisasi menggunakan Differential Thermal Analysis (DTA), Powder X-Ray Diffraction (PXRD), Scanning Electron Microscope (SEM), and Fourier Transforms Infrared Spectrophotometer (FTIR), serta dilakukan juga uji disolusi secara *in-vitro*. Data termogram menunjukkan adanya puncak endotermik baru pada 277,9 °C. Puncak-puncak baru pada 2θ 9,81, 12,99, and 19,80° terlihat dari difraktogram Co Qu-Ma. Citra SEM menunjukkan bahwa masing-masing Kristal Qu dan Ma berbentuk columnar-shaped dan pebble-shaped. Bilangan gelombang gugus fungsi O-H bergeser dari 3411 menjadi 3428 dan 3418 cm^{-1} untuk masing-masing campuran fisik (pm) Qu-Ma dan Co Qu-Ma. Hasil karakterisasi sifat fisikakimia di atas menunjukkan bahwa Co Qu-Ma berhasil dibuat menggunakan metode evaporasi pelarut. Uji disolusi secara *in-vitro* menunjukkan bahwa Co Qu-Ma mempunyai laju disolusi sebesar 95,30% pada menit ke-60. Kokristal secara efektif mampu meningkatkan laju disolusi dan efisiensi disolusi jika dibandingkan dengan kuersetin murni dan campuran fisik (pm) Qu-Ma.

Kata Kunci: kuersetin; asam malonat; kokristal; disolusi *in-vitro*

INTRODUCTION

Quercetin is a flavonoid, which can be found in citrus fruits, tea, onions, apple and berry [1]. These plant substances were also well known as an antioxidant, which prevent the damage made by free radicals [2]. Moreover, it is reported that quercetin exhibits other pharmacological effects such as anticancer, cardio protectant, antibacterial and antiviral activity [2-5]. The solubility of quercetin in water is

0.3 $\mu\text{g}/\text{mL}$ [3], the bioavailability of quercetin is considered low due to its poor water solubility [2,5]. In addition, this poor water solubility also limits the dissolution process, which is the rate-limiting step in the absorption process.

Cocrystals formation is one of the methods used to improve the solubility and dissolution rate of poorly soluble drug. Cocrystals are a complex of two, or more, neutral compounds linked each other in the crystal lattice through non-covalent bond [6]. Moreover,

* Corresponding author.
Email address : dwisetawan-90@ff.unair.ac.id

cocrystallization improves the hygroscopicity, chemical stability, compressibility, and flow properties of the compound [6-8]. It has been reported that quercetin cocrystals were successfully produced using several cofomers such as caffeine, isonicotinamide and theobromine. Previous finding showed that cocrystallization with caffeine increased water solubility of quercetin up to 8 times compared to the pure quercetin [8-13]. Nevertheless, none has been reported for the cocrystallization of quercetin with malonic acid as cofomer.

This study was aimed to produce quercetin cocrystals with malonic acid as a cofomer at 1:2 molar ratios using solvent evaporation method. Malonic acid is a cofomer possessing carboxylic group, which possibly bind the hydroxyl group of quercetin through hydrogen bond to form cocrystals [12,14]. Moreover, malonic acid is considered safe to be used as a cofomer since it is classified as Generally Regarded as Safe (GRAS) compound. The cocrystals obtained were characterized for the physicochemical characteristics and the dissolution rate profile was examined.

EXPERIMENTAL SECTION

Materials

The following materials were used in this study quercetin monohydrate (Tokyo Chemical Industry, Tokyo, Japan, Lot 83N20), malonic acid (E-Merck, Germany), ethanol pro-analysis (E-Merck, Germany), potassium bromide, citric acid, sodium hydroxide, sodium lauryl sulfate (Sigma-Aldrich, Germany), and distilled water.

Instrumentation

The instruments used were differential thermal analyzer (DTA, Mettler Toledo FP85 TA Cell, Polaris Parkway Columbus, USA), powder X-Ray diffraction (PXRD, Phillips X'Pert, PANalytical, Almelo, Netherlands), Scanning Electron Microscope (SEM, Jeol JSM-7900F, Tokyo Japan), Fourier Transforms Infrared Spectrophotometer (FTIR, Spectrum One, Perkin Elmer, Massachusetts, USA), dissolution apparatus (Erweka DT 700, Heusenstamm, Germany) and UV-Vis spectrophotometer (Cary 50 Conc. Varian®, San Diego, California, USA).

Procedure

Formation of quercetin-malonic acid cocrystal (Co Qu-Ma)

Quercetin (Qu) and malonic acid (Ma) were dissolved separately in ethanol at 1:2 molar ratios. Both

solutions were mixed with the aid of magnetic stirrer and solvent was then evaporated. Dried powder was homogenized and kept in desiccator for 48 h prior to analysis.

Physicochemical characterization

Differential Thermal Analysis (DTA) method. Endothermic peak of Qu, Ma, physical mixture (Pm) Qu-Ma and cocrystals (Co) Qu-Ma were measured using DTA (Mettler Toledo FP85 TA Cell, Polaris Parkway Columbus, USA). Approximately 5 to 10 mg of sample was put into the DTA crucible pan and pressed so that the container was closed. DTA temperature range was set from 30–350°C (temperature increment 10 °C/min).

Powder X-Ray Diffraction (PXRD). Powder X-ray diffraction and diffraction peaks of Qu, Ma, and their physical mixtures were measured using PXRD (Phillips X'Pert, PANalytical, Almelo, Netherlands). Diffraction angles 2θ were set at 5–50°. The electricity was set at 40 kV, 40 mA. Analysis was conducted at room temperature.

Scanning Electron Microscopy (SEM). Analysis using scanning electron microscope was conducted to examine the crystal morphology of quercetin monohydrate, malonic acid, and the cocrystals. Approximately 10 mg samples were sealed with 10 nm thick gold plate. Samples were placed in a specimen stub and observed at several magnifications using SEM (Jeol JSM-7900F, Tokyo Japan).

Fourier Transforms Infrared Spectrophotometry (FTIR). The infrared spectra of Qu, Ma, Pm Qu-Ma and Co Qu-Ma were obtained by using IR spectrophotometer FTIR (Spectrum One, Perkin Elmer, Massachusetts, USA). Approximately 10 mg samples were homogenized with potassium bromide. Samples were put into a vacuum dryer and pressed to produce potassium bromide disk. The disk was placed in sample holder and examined at wavenumber 400–4000 cm^{-1} .

In vitro dissolution study

In vitro dissolution study of Qu, Pm Qu-Ma and Co Qu-Ma were performed using type II (paddle type) dissolution apparatus (Erweka DT 700, Heusenstamm, Germany). Citric-sodium hydroxide buffer 900 mL, pH 5 \pm 0.05 with 2% sodium lauryl sulphate (SLS) obtained at 37 °C \pm 0.5 °C was used as dissolution media. The stirring speed was set at 100 rpm. Sample equivalent to 20 mg quercetin monohydrate was placed into the dissolution chamber. Samples, 5 mL each, were taken periodically at 5, 10, 15, 30, 45 and 60 min and then replaced by the same volume of media. The samples were filtered through membrane filter (0.45 μm , Merck Millipore, USA) and the absorbance were measured

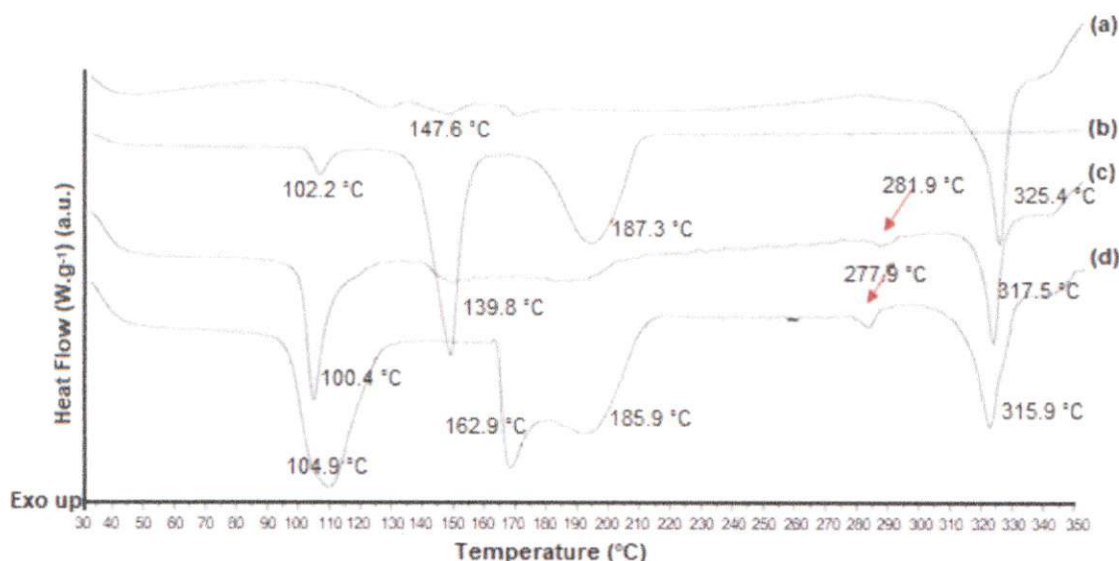


Fig 1. Thermogram DTA of Qu (a); Ma (b); Pm Qu-Ma (c) and Co Qu-Ma (d). The arrow indicates new peak observed in physical mixture as well as in the cocrystals

using UV-Vis spectrophotometer (Cary 50 Conc. Varian®, San Diego, California, USA), at the maximum wavelength of quercetin 366.95 nm. The percentage of quercetin dissolved from each sample was analyzed, and the percentage of dissolution efficiency at 60 min was calculated.

RESULT AND DISCUSSION

Differential Thermal Analysis

Fig. 1 shows the thermogram of Qu, Ma, Pm Qu-Ma and Co Qu-Ma. The thermogram of Qu showed endothermic peaks at 147.6 °C representing dehydration process, and at 325.4 °C [Fig. 1a]. The thermogram of Ma showed endothermic peaks at 102.2 °C representing dehydration process, at 139.7 °C representing the melting point of Ma, and at 187.3 °C showing the decomposition of Ma [Fig. 1b]. The thermogram of Pm Qu-Ma showed endothermic peaks at 100.4 °C representing dehydration process, at 317.5 °C representing the melting point of Qu, and a new peak at 281.9 °C [Fig. 1c]. The thermogram of Co Qu-Ma showed endothermic peaks at 104.9 °C representing dehydration process, at 162.9 °C representing peak of Ma, at 185.9 °C showing the decomposition of Ma, at 315.9 °C representing peak of Qu, and a new peak at 277.9 °C [Fig. 1d].

The thermogram of Co Qu-Ma showed an endothermic peak at 277.9 °C which is higher when compared to that of Ma and is lower when compared to that of Qu. The shifting of the melting point indicates the possible interaction between components to form cocrystals [2,9,11,14]. One of the parameter used to

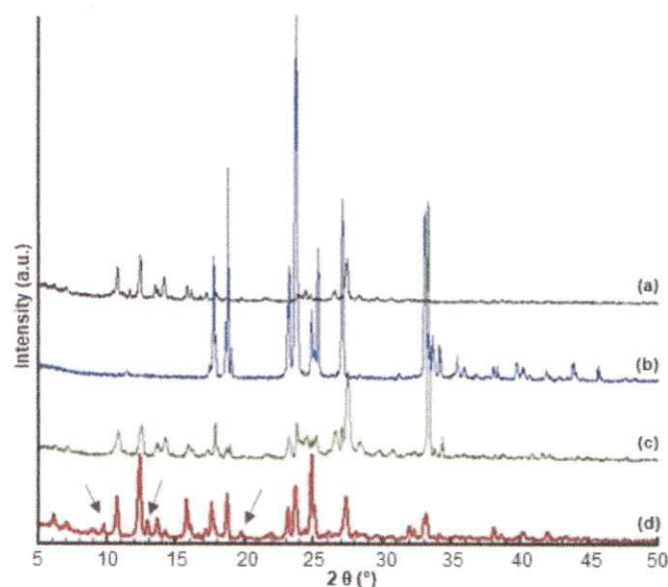


Fig 2. Diffractogram of Qu (a); Ma (b); Pm Qu-Ma (c) and Co Qu-Ma (d). The arrows indicate new peaks observed in the cocrystals

assess the formation of cocrystals is melting point. The appearance of new melting point positioned between the melting points of cocrystals components may clarify the cocrystals formation. This is in agreement with previous studies on fluoxetine hydrochloride - L-tartaric acid [7] and artesunate-nicotinamide [11].

Powder X-Ray Diffraction

The diffractogram of Qu exhibited sharp and specific peaks at 5.46; 6.22; 7.08; 10.78; 12.43; 13.52;

14.15; 15.84; 24.78; 26.44; and 27.41° [2,4] as seen on Fig. 2a. Furthermore, the diffractogram of Ma exhibited sharp and specific peaks at 17.77; 18.79; 23.24; 23.77; 25.31; 27.10; and 33.63° (Fig. 2b). The Pm Qu-Ma diffractogram showed most of peak from quercetin and malonic acid (Fig. 2c). There is no new or previously unidentified peak presented by the diffractogram of the physical mixture. The diffractogram of Co Qu-Ma showed new diffraction peaks at 9.81; 12.99; and 19.80° (Fig. 2d).

Furthermore, the formation of new crystal lattice in cocrystallization product was clarified using powder X-ray diffraction analysis. The formation of cocrystal is confirmed by the appearance of new peak in the diffractogram [2,7,9,11,14]. The large number of sharp and specific peaks shown by Qu and Ma indicates the unique crystalline form of these compounds [9,15]. The diffractogram of the physical mixture showed a superposition of diffraction peaks of the components compared to the original Qu as well as Ma. This result suggests that there is no interaction between Qu and Ma in the physical mixture. On the other hand, the diffractogram of Co Qu-Ma showed new diffraction peaks at 9.81, 12.99, and 19.80° which are not identified in the diffractogram of pure components or physical

mixture, this result indicates the successful formation of Co Qu-Ma [2,7,9,14-15].

Scanning Electron Microscopy

In this study, observations on the crystal morphology of Qu, Ma and Co-Qu-Ma were conducted at 1500 and 2500 magnifications, whilst the observation on the crystal morphology of malonic acid was conducted at the lower magnifications (300 and 600 x), due to its large crystal size. The SEM results in Fig. 3 showed that Qu exhibited a columnar shaped with non-uniform crystal size. Ma exhibited a pebble-shaped crystal with particle size approximately 300 µm (observed at 300 magnifications) [14]. The Co Qu-Ma exhibited the same crystal shape as malonic acid but covered with quercetin crystals in uniform size. The data is presented by photomicrograph at 300 x and 600 x magnifications.

The cocrystallization product exhibits a change in the external structure and morphology of the crystal [2,11,14]. In this study, observations on the crystal of Qu, Ma and Co Qu-Ma were conducted at different magnifications. The lower magnifications were used to observe Ma crystal since the crystal size is larger than

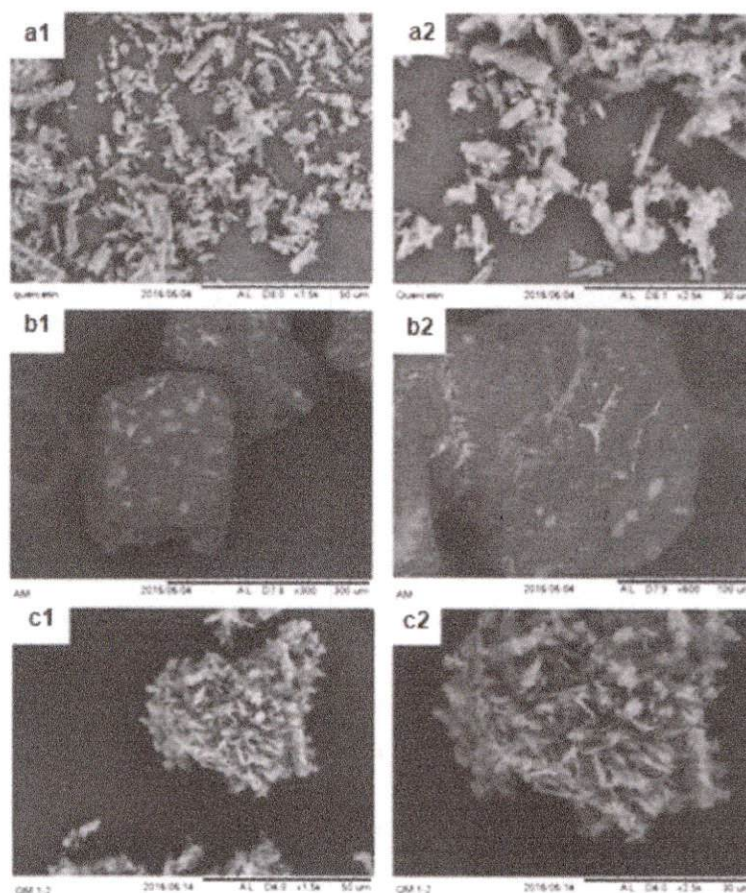


Fig 3. SEM of Qu, Ma and Co Qu-Ma in 300× magnification (a1, b1, c1), and in 600× magnification (a2, b2, c2)

other samples [14]. The Co Qu-Ma exhibited the form of Ma crystal covered by Qu crystal. These results suggest a weak intermolecular interaction between Qu and Ma in the formation of Co Qu-Ma.

Fourier Transforms Infrared Spectroscopy (FTIR)

The FTIR spectra for the pure Qu, Ma, Physical Mixture Qu-Ma and cocrystal are shown in Fig. 4. In the FTIR spectrum of Qu, absorbance at 3411 cm^{-1} was assigned to a free -OH bond vibration, at 1667 cm^{-1} and 1612 cm^{-1} were assigned to the stretching vibration of C=O group at 1522 cm^{-1} was assigned to an aromatic group, at 1319 cm^{-1} and 1168 cm^{-1} were assigned to the C-O-C vibration, and at 1000 cm^{-1} was assigned to the aromatic group bending vibration. In the FTIR spectrum of Ma, there were absorbance of O-H stretching at 3418 cm^{-1} to 2952 cm^{-1} , and C=O stretching of carboxylic acid at 1731 cm^{-1} .

FTIR spectrum of the physical mixture showed O-H stretching at 3428 cm^{-1} and C=O stretching of carboxylic acid at 1667 cm^{-1} . The shift in the FTIR spectra found in cocrystal at wavenumber 3418 cm^{-1} for the -OH group and at wavenumber range of 1666 cm^{-1} to 1612 cm^{-1} for a carboxyl group stretching showed the formation of hydrogen bonds between quercetin and malonic acid [2,7,14,16].

FTIR spectral analysis was conducted to examine the possible intermolecular interaction between Qu and Ma in the formation of CoQu-Ma. Hydrogen bonding, one of non-covalent bonding, is involved in the formation of cocrystal. The formation of cocrystal potentially shifts the peak, decreases the peak intensity, diminishes peak and produces new peaks in FTIR spectra [2,10,12]. The result showed that Pm Qu-Ma and Co Qu-Ma slightly shifted the IR band of -OH functional group of quercetin. Nevertheless, there is no significant different in the IR bands of C-O-C and aromatic functional group from IR spectra of physical mixture when compared to those of quercetin-malonic acid cocrystals. These results indicate an intermolecular interaction between components in the formation of quercetin-malonic acid co-crystal.

In vitro Dissolution Test

The percentage of Qu dissolved is shown in Fig. 5. The dissolution Qu in pure Qu as well as in physical mixture of Qu-Ma were similar with the dissolution rate obtained less than 65% at 60 min. Cocrystal of Qu-Ma showed higher percentage of quercetin dissolved, which reached 95.30% at 60 min. Furthermore, *in vitro* dissolution rate of quercetin in the cocrystal of Qu-Ma was the highest compared to the pure Qu as well as physical mixture of Qu-Ma.

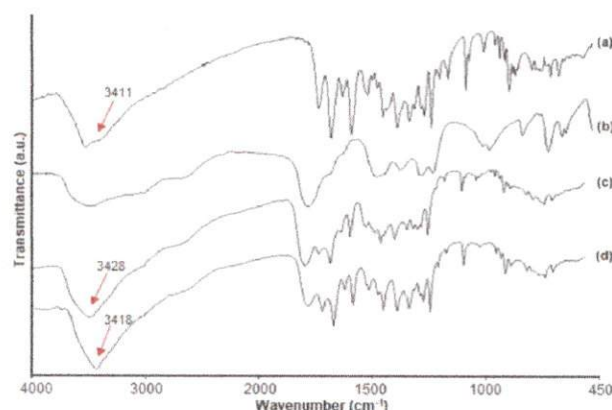


Fig 4. FTIR spectra of Qu (a), Ma (b), PmQu-Ma (c) and Co Qu-Ma (d)

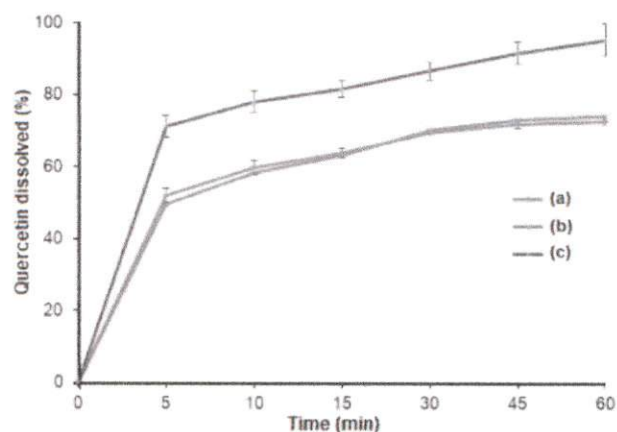


Fig 5. Dissolution profile of (a) Qu, (b) Pm Qu-Ma, and (c) Co Qu-Ma ($n = 3$)

The dissolution test was performed to compare the dissolution profile of Pm Qu-Ma and Co Qu-Ma. The dissolution profile of Qu showed poor dissolution, and there was no significant difference between the dissolution rate of Qu and that of Pm Qu-Ma. The results of dissolution test can also be expressed by percentage of dissolution efficiency (% DE), which is total of drug dissolved in the dissolution media during dissolution test. This parameter completely describes dissolution process of a compound [2,17-18]. The dissolution efficiency (% DE) can be determined by measuring area under curve (AUC) obtained from the dissolution curve. Qu exhibited poor dissolution efficiency with % DE of $64.46 \pm 0.93\%$, whilst Pm Qu-Ma exhibited slightly higher dissolution efficiency with % DE of $64.56 \pm 0.26\%$. The Pm Qu-Ma system showed no significant change as compared to the pure Qu. Co Qu-Ma significantly increased the dissolution efficiency (% DE) was $82.57 \pm 2.81\%$. These results indicate that Co Qu-Ma increased the dissolution rate of quercetin. Some mechanisms may be involved in the improvement of dissolution rate of quercetin in

cocrystals system, for example, solubilization of the coformer malonic acid, which is a water-soluble compound [3]. It is reported that decrease in lattice energy and increase in the solvent affinity to cocrystal may also increase the dissolution rate [2-3,17-18].

CONCLUSION

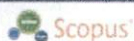
The physicochemical characterizations using DTA, PXRD, SEM, and FTIR indicated that quercetin-malonic acid cocrystals were successfully obtained through solvent evaporation method. These cocrystals effectively increased dissolution rate and dissolution efficiency compared to the pure quercetin and physical mixture of quercetin-malonic acid.

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REFERENCES

- [1] Kaur, H., and Kaur, G., 2014, A critical appraisal of solubility enhancement techniques of polyphenols, *J. Pharm.*, 2014, 180845.
- [2] Setyawan, D., Oktavia, I.P., Farizka, R., and Sari, R., 2017, Physicochemical characterization and in vitro dissolution test of quercetin-succinic acid cocrystals prepared using solvent evaporation, *Turk. J. Pharm. Sci.*, 14 (3), 280–284.
- [3] Smith, A.J., Kavuru, P., Wojtas, L., Zaworotko, M.J., and Shytle, R.D., 2011, Cocrystals of quercetin with improved solubility and oral bioavailability, *Mal. Pharmaceutics*, 8 (5), 1867–1876.
- [4] Setyawan, D., Fadhil, A.A., Juwita, D., Yusuf, H., and Sari, R., 2017, Enhancement of solubility and dissolution rate of quercetin with solid dispersion system formation using hydroxypropyl methyl cellulose matrix, *Thai J. Pharm. Sci.*, 41 (3), 112–116.
- [5] Dian, L., Yu, E., Chen, X., Wen, X., Zhang, Z., Qin, L., and Wu, C., 2014, Enhancing oral bioavailability of quercetin using novel soluplus polymeric micelles, *Nanoscale Res. Lett.*, 9 (1), 684.
- [6] Najar, A.A., and Azim, Y., 2014, Pharmaceutical cocrystals: A new paradigm of crystal engineering, *J. Indian Inst. Sci.*, 94 (1), 45–68.
- [7] Parmar, V.K., and Shah, S.A., 2013, Hydrochloride salt co-crystals: Preparation, characterization and physicochemical studies, *Pharm. Dev. Technol.*, 18 (2), 443–453.
- [8] Vasisht, K., Chadha, K., Karan, M., Bhalla, Y., Jena, A.K., and Chadha, R., 2016, Enhancing biopharmaceutical parameters of bioflavonoid quercetin by cocrystallization, *CrystEngComm*, 18, 1403–1415.
- [9] Veverka, M., Dubaj, T., Gallovič, J., Jorík, V., Veverková, E., Danihelová, M., and Šimon P., 2015, Cocrystals of quercetin: Synthesis, characterization, and screening of biological activity, *Monatsh. Chem.*, 146 (1), 99–109.
- [10] Sekhon, B.S., 2012, Nutraceutical cocrystals: An overview, *RGUHS J. Pharm. Sci.*, 2, 16–25.
- [11] Setyawan, D., Sari, R., Yusuf, H., and Primaharinastiti, R., 2014, Preparation and characterization of artesunate-nicotinamide cocrystal by solvent evaporation and slurry method, *Asian J. Pharm. Clin. Res.*, 7 (1), 62–65.
- [12] Espinosa-Lara, J.C., Guzman-Villanueva, D., Arenas-García, J.I., Herrera-Ruiz, D., Rivera-Islas, J., Román-Bravo, P., Morales-Rojas, H., and Höpfl, H., 2012, Cocrystals of active pharmaceutical ingredients-Praziquantel in combination with oxalic, malonic, succinic, maleic, fumaric, glutaric, adipic, and pimelic acids, *Cryst. Growth Des.*, 13 (1), 169–185.
- [13] Xu, L.L., Chen, J.M., Yan, Y., and Lu, T.B., 2012, Improving the solubility of 6-mercaptopurine via cocrystals and salts, *Cryst. Growth Des.*, 12 (12), 6004–6011.
- [14] Wicaksono, Y., Setyawan, D., and Siswandono, S., 2017, Formation of ketoprofen-malonic acid cocrystal by solvent evaporation method, *Indones. J. Chem.*, 17 (2), 161–166.
- [15] Sarkar, A., and Rohani, S., 2015, Cocrystals of acyclovir with promising physicochemical properties, *J. Pharm. Sci.*, 104 (1), 98–105.
- [16] Kakran, M., Sahoo, N.G., Li, L., and Judeh, Z., 2012, Fabrication of quercetin nanoparticles by anti-solvent precipitation method for enhanced dissolution, *Powder Technol.*, 223, 59–64.
- [17] Thakuria, R., Delori, A., Jones, W., Lipert, M.P., Roy, L., and Rodríguez-Hornedo, N., 2013, Pharmaceutical cocrystals and poorly soluble drugs, *Int. J. Pharm.*, 453 (1), 101–125.
- [18] Surov, A.O., Voronin, A.P., Manin, A.N., Manin, N.G., Kuzmina, L.G., Churakov, A.V., and Perlovich, G.L., 2014, Pharmaceutical cocrystals of diflunisal and diclofenac with theophylline, *Mol. Pharmaceutics*, 11 (10), 3707–3715.



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