

PREPARATION OF ACYCLOVIR-ISONICOTINAMIDE COCRYSTAL BY SOLVENT EVAPORATION METHOD WITH METHANOL AND ISOPROPANOL

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ABSTRACT

PREPARATION OF ACYCLOVIR-ISONICOTINAMIDE COCRYSTAL BY SOLVENT EVAPORATION METHOD WITH METHANOL AND ISOPROPANOL. Acyclovir is a nucleoside synthetic analog antiviral group used in the treatment of Herpes simplex virus (HSV-1 & HSV-2) and Varicella zoster virus (VZV). Acyclovir has low water solubility, so it needs to be modified in the form of cocrystal with isonicotinamide. This study aims to obtain the physical characteristics produced by acyclovir-isonicotinamide cocrystal (1:1) made through the solvent evaporation method with methanol and isopropanol. The crystalline formed is characterized by DSC, PXRD, FT-IR and SEM. The characterization results showed the presence of new crystals that formed between acyclovir-isonicotinamide in methanol and isopropanol solvents. Thermograms showed sharp exothermic peaks at 183.31°C and 186.24°C. The diffractogram showed a new peak at $2\theta = 5.19$ and 5.82. The spectrum showed a shift in wavelength in the cocrystal formed. The cocrystal has a different morphology compared with parent drug and coformer on analysis using SEM. This research shows that acyclovir can form cocrystal with isonicotinamide by solvent evaporation method with methanol and isopropanol.

Keywords: Acyclovir, Cocrystal, Isonicotinamide, Solvent Evaporation

ABSTRAK

PEMBENTUKAN KOKRISTAL ASIKLOVIR-ISONIKOTINAMIDA DENGAN METODE PENGUAPAN PELARUT MENGGUNAKAN PELARUT METANOL DAN ISOPROPANOL. Asiklovir adalah nukleosida sintetik yang merupakan analog kelompok antivirus, digunakan dalam pengobatan penyakit akibat virus Herpes simplex (HSV-1 dan HSV-2) dan Varicella zoster (VZV). Asiklovir memiliki kelarutan dalam air yang rendah sehingga memerlukan modifikasi bentuk kristal dengan bantuan isonikotinamida. Penelitian ini bertujuan untuk mendapatkan karakteristik fisika kokristal asiklovir-isonikotinamida (1:1) yang dibuat menggunakan metode penguapan pelarut dengan metanol dan isopropanol. Padatan kristalin dikarakterisasi menggunakan instrumen DSC, PXRD, FT-IR dan SEM. Termogram memperlihatkan puncak eksotermik tajam pada temperatur 183,31oC dan 186,24oC. Difraktogram menunjukkan puncak baru pada sudut $2\theta = 5,19\text{o}$ dan 5,82o. Spektra infra merah mengilustrasikan pembentukan padatan kristal baru melalui pergeseran bilangan gelombang. Kokristal menggambarkan perbedaan morfologi bila dibandingkan dengan asiklovir dan isonikotinamida tunggal menggunakan SEM. Dapat disimpulkan bahwa asiklovir dapat membentuk kokristal bersama dengan isonikotinamida pada perbandingan 1:1 menggunakan metode penguapan pelarut dengan metanol dan isopropanol.

Kata kunci: Asiklovir, Kokristal, Isonikotinamida, Penguapan Pelarut

INTRODUCTION

Acyclovir is an antiviral that is widely used for herpes therapy caused by HSV-1 and HSV-2 and in varicella zoster virus therapy. Acyclovir has a specific mechanism of action so that it has low toxicity [1,2].

Acyclovir is a drug included in class 4 BCS (*Biopharmaceutics Classification System*) because it has low bioavailability and solubility. The oral bioavailability of acyclovir is 10-30% and has a water

solubility of 1.3 mg/mL at 25°C [3,4]. Some efforts that can be done to improve the solubility and bioavailability of drugs in the body include micronization, solubilization, making salt form, making complex with polymer, prodrug and derivatization, cocrystallization [5].

Cocrystal formation is a method that can be used to improve the solubility and bioavailability of a drug. Any form of drug can potentially be used as cocrystal. Cocrystal is the formation of bonds between active ingredients and coformer which are suitable through non-covalent bonds such as hydrogen, pi, and Van der Waals bonds [6,7]. Cocrystal formation can change the composition of a material in a molecular manner and can improve the physicochemical properties of drug ingredients without changing the intrinsic properties of a material [6,8].

In this study, the formation of acyclovir cocrystal using isonicotinamide (1:1) as a coformer by the solvent evaporation method with methanol and isopropanol. Isonicotinamide has electron donor groups and acceptor groups that can hold hydrogen bonds [9], [10]. A study on dexlansoprazole which is made into cocrystal with isonicotinamide (1:1) has a higher solubility than pure dexlansoprazole [10]. In addition, the dielectric constant values of methanol and isopropanol are 32,8 and 18,3, respectively [11]. The difference in dielectric constant of the solvent can affect the physical characteristics of the resulting cocrystal.

Based on the above, it is very important to prepare cocrystal between acyclovir and isonicotinamide, so it can improve physicochemical characteristics of acyclovir. The crystalline obtained will be characterized by PXRD (Powder X-Ray Diffraction), DSC (Differential Scanning Calorimetry), FT-IR (Fourier-Transform Infrared Spectroscopy), and SEM (Scanning Electron Microscopy).

EXPERIMENTAL METHOD

Materials and Instruments

The materials used in this study are acyclovir (Sigma Aldrich®.US), Isonicotinamide (Sigma Aldrich®,US), methanol and isopropanol, Emsure® (Merck, Germany).

Method and Procedure

Preparation of Binary System Acyclovir and Isonicotinamide.

Acyclovir and isonicotinamide were sieved to get the same particle size. Acyclovir and isonicotinamide are weighed based on molar ratio (10: 0; 9: 1; 8: 2; 7: 3; 6: 4; 5: 5; 4: 6; 3: 7; 2: 8; 1: 9; 0 : 10) then mixed physically in the mortar. The melting point at each comparison is

determined using DSC then used to make the phase diagram of the acyclovir - isonicotinamide binary system.

Preparation of Cocrystal Acyclovir–Isonicotinamide By Solvent Evaporation

225 mg of acyclovir and 112 mg of isonicotinamide (ratio 1:1) are then dissolved into each solvent (methanol). Acyclovir and isonicotinamide solutions are mixed into a cup and stirred using a magnetic stirrer overnight at room temperature until crystals form. The crystals that are formed are collected and then put into vials and stored under conditions of low humidity (~40%). The formed crystals used for physical characterization. The same method for isopropanol (solvent).

Differential Scanning Calorimetry (DSC)

Thermal analysis is carried out using DSC to determine the melting and crystallization points. Samples were weighed 5-7 mg then analyzed using DSC (Mettler Toledo DSC 1 Star® System, Switzerland) in the temperature range of 30-300 °C with an increase of 5°C/min.

Powdered X-Ray Diffraction (PXRD)

The crystal structure was analyzed using PXRD (Philip X'Pert, Netherland) with the target conditions Cu, filter K α , voltage 40kV, 15-30mA carried out at 2 θ 5-40 ° at 25 °C.

Fourier Transformed Infrared (FT-IR)

Samples were mixed with KBr (potassium bromide) in a ratio of 1% w/w. the mixture was analyzed using FTIR (Jasco FT-IR/5300, Japan) at a wavelength of 400-4000/cm.

Scanning Electron Microscopy (SEM)

The sample is placed in the sample container and coated with gold aluminum with a thickness of 10 nm. Samples were observed at various magnifications using SEM (FEI Inspect 550, USA) which was regulated with a voltage of 20kV and 12 mA.

RESULT AND DISCUSSION

DSC is thermal analysis method to evaluate changes in thermodynamic properties that occur when the material supplied heat energy. Changes can be observed in the process of melting, recrystallization or solid phase transformations indicated by endothermic or exothermic peaks [11].

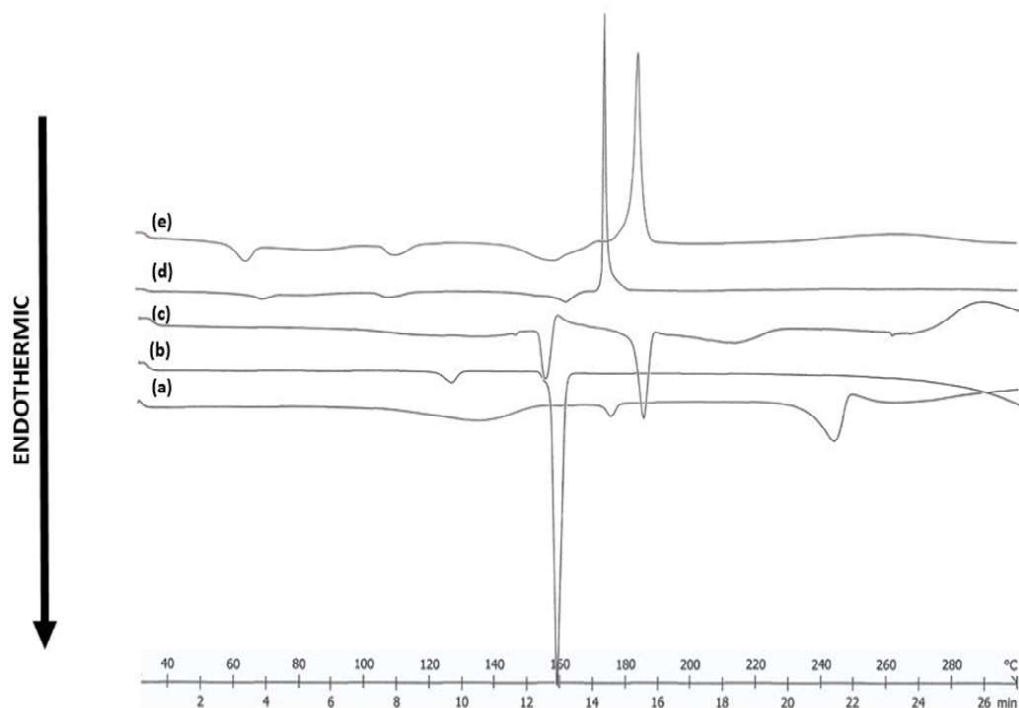


Figure 1. Figure 1. DSC thermogram comparison of acyclovir (A), isonicotinamide (B), physical mixture of acyclovir-isonicotinamide (1: 1) (C), and two cocrystal with methanol (D), and isopropanol (E) solvent.

Thermogram (Figure 1) shows different peaks between acyclovir, isonicotinamide, physical mixture, and cocrystal. Sharp exothermic peaks were formed of methanol and isopropanol cocrystal at 183.31 °C and 186.24 °C. This exothermic peak is caused by decomposition in the form of oxidation from cocrystal [12]. While the endothermic peak in methanol cocrystal and isopropanol cocrystal

at 107.09°C and 109.10°C is caused by crystalline water that evaporates at that temperature or dehydration occurs [13,14]. The difference in melting point between the acyclovir, isonicotinamide, physical mixture and cocrystal indicates the formation of new crystals.

The diffractogram in Figure 2 indicated new peaks in cocrystal methanol at $2\theta = 5.19; 14.05; \text{ and } 14.91$. While

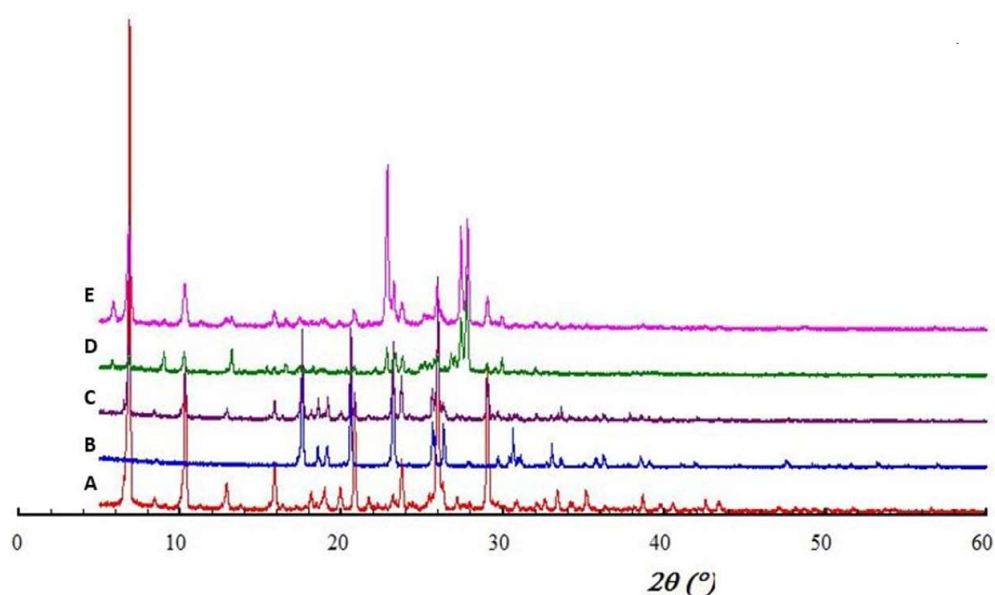


Figure 2. Diffractogram of acyclovir (A), isonicotinamide (B), physical mixture of acyclovir-isonicotinamide (1:1) (C), cocrystal of acyclovir-isonicotinamide (1:1) (methanol) (D), and cocrystal of acyclovir-isonicotinamide (1:1) (isopropanol) (E).

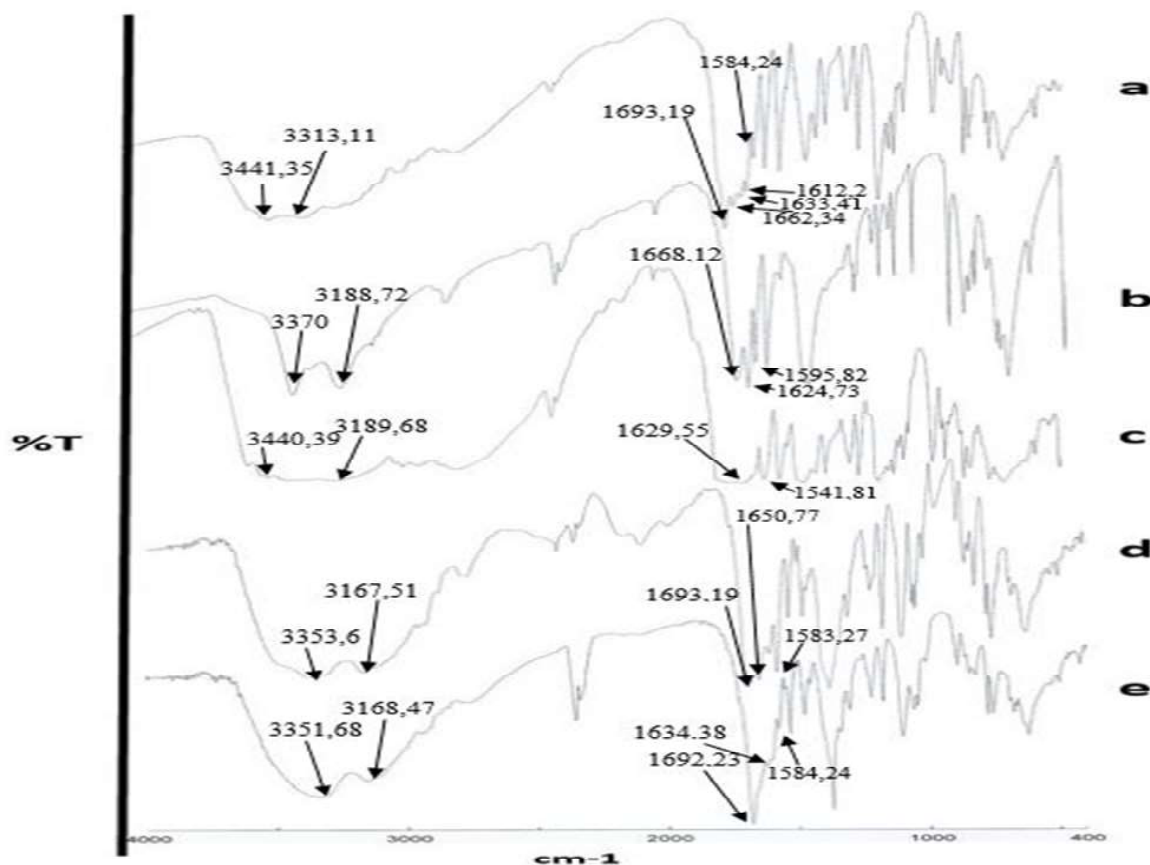


Figure 3. Infrared spectrum of acyclovir (A), isonicotinamide (B), physical mixture of acyclovir-isonicotinamide (C) and two types of cocrystal with methanol (D), and isopropanol (E) solvent.

in isopropanol, cocrystal are at $2\theta = 5.82$. Both cocrystal had new diffractogram peaks which were not present on the diffractogram of acyclovir, isonicotinamide, and physical mixture (1:1). The presence of a new diffractogram and the loss of several existing diffractograms on acyclovir, isonicotinamide, and physical mixture indicate that cocrystal is formed [7], [14,15].

FTIR spectrum readings were carried out in the wavelength range of 4000-400/cm and can be seen in Figure 3. There is a shift of primary N-H and secondary N-H from cocrystal with methanol or isopropanol as a solvent when compared with pure acyclovir crystals. The primary N-H of acyclovir is from 3441 cm⁻¹ shifted to 3353 cm⁻¹ in cocrystal with methanol and 3351 cm⁻¹ in cocrystal with isopropanol. The secondary N-H group shifted from 3313 cm⁻¹ to 3167 cm⁻¹ in cocrystal with methanol as a solvent and 3168 cm⁻¹ in cocrystal with isopropanol. The existence of N-H shift indicates the formation of hydrogen bonds as result of the formation of cocrystal. This hydrogen bonding occurs because of an interaction between the hydrogen donor and the hydrogen acceptor of the active ingredient and the cofomer. Whereas in the physical mixture the N-H and C=O peaks were not observed because the pellets that were read in the FT-IR underwent a process of pressing up to

2 times. The pressing process will energize the physical mixture so that it can affect readings on the FT-IR spectrum [7,16,17].

The photomicrograph analysis (SEM) in Figure 4 showed a change in the shape of the acyclovir, isonicotinamide, physical mixture and cocrystal. The crystalline form of acyclovir is long, thin, and resembles a knife with sharp angles. Isonicotinamide has a column shape, visible particles long, wide, with a rough surface and has rounded corners. The physical mixture is the form of acyclovir and on the surface of acyclovir is shaped like a blade, there are small particles attached to the surface. Photomicrographs showed no significant differences in cocrystal with methanol and isopropanol solvents. Cocrystal with methanol as a solvent has a long column (needle shape) of crystalline shape with an angular tip, while in the use of isopropanol, the column is shorter than methanol cocrystal. In another study using isopropanol as a solvent to form dipivoxyl-saccharin cocrystal also gave a needle-shaped crystals. The crystal habit change may affect their mechanical properties, which is worthy of further studies [18].

The acyclovir-isonicotinamide (1:1) cocrystal with methanol gave more new diffractogram peaks compared to isopropanol and it is more homogenous in terms of crystal composition.

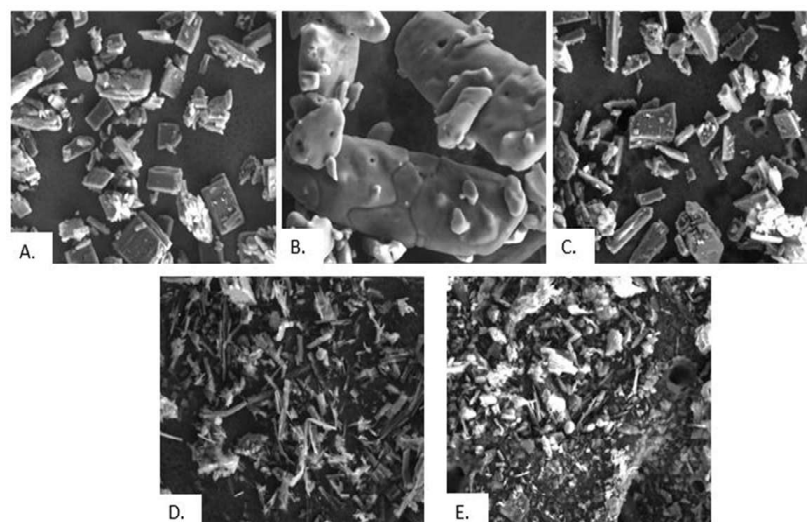


Figure 4. SEM of acyclovir (A), isonicotinamide (B), physical mixture of acyclovir-isonicotinamide (C) and two types of cocrystal with methanol (D), and isopropanol (E) solvent with magnification 1000x.

CONCLUSION

Based on the results, it can be concluded that acyclovir-isonicotinamide (1:1) cocrystal can be formed using methanol and isopropanol solvents through the solvent evaporation method. Cocrystal is formed from this study supported by characterization using DSC, PXRD, FTIR, and SEM. The formed cocrystal of acyclovir-isonicotinamide showed different physicochemical characteristics compared to the constituent materials. Cocrystal which were prepared by using methanol gave more new diffractogram peaks compared to isopropanol and it is more homogenous in terms of crystal composition. For further research, it is possible to carry out solubility test to show that the cocrystal formed has a good bioavailability.

REFERENCES

- [1] W. E. Benitz, "Infectious Disease and Pharmacology: Neonatology Questions and Controversies", *Elsevier Heal. Sci.*
- [2] K. Robert, M and B. Stanton, *Nelson Textbook of Pediatrics volume 2*. Elsevier Health Sciences., 2016.
- [3] R. Cortesi, L. Ravani, E. Menegatti, M. Dreschsler, and E. Esposito, "Colloidal Dispersions for the Delivery of Acyclovir: A Comparative Study", *Indian J. Pharm. Sci.*, vol. 73, no. 6, pp. 687–93, 2011.
- [4] American Hospital Formulary, *AHFS Drug Information*. 2008.
- [5] B. Gill, T. Kaur, S. Kumar, and G. D. Gupta, "Formulation and evaluation of glimepiride solid dispersion tablets", *Asian J. Pharm.*, vol. 4, no. 3, pp. 212–218, 2010.
- [6] S. Yadav, prakash chandra Gupta, N. Sharma, and J. Kumara, "Cocrystals/ : An Alternative Approach to Modify Physicochemical Properties of Drugs", *Int. J. Pharm. Chem. Biol. Sci.*, vol. 4, no. March, 2015.
- [7] Y. Wicaksono, D. Setyawan, and Siswandono, "Formation of ketoprofen-malonic acid cocrystal by solvent evaporation method", *Indones. J. Chem.*, vol. 17, no. 2, pp. 161–166, 2017.
- [8] A. N. Allam, V. F. Naggat, and S. S. El Gamal, "Formulation and physicochemical characterization of chitosan/Acyclovir cocrystals", *Pharm. Dev. Technol.*, vol. 18, no. 4, pp. 856–865, 2013.
- [9] Y. Kang, J. Gu, and X. Hu, "Syntheses, structure characterization and dissolution of two novel cocrystals of febuxostat", *J. Mol. Struct.*, vol. 1130, pp. 480–486, 2017.
- [10] J. Li *et al.*, "Improving the solubility of dexlansoprazole by cocrystallization with isonicotinamide", *Eur. J. Pharm. Sci.*, vol. 85, pp. 47–52, 2016.
- [11] P.J. Sinko, Martin, N. Alfred, *Martin's Physical Pharmacy and Pharmaceutical Sciences: Physical Chemical and Biopharmaceutical Principles in the Pharmaceutical Sciences*. Lippicott Williams & Wilkins, 2011.
- [12] A. N. Winantari, D. Setyawan, S. Siswodihardjo, and S. N. Soewandhi, "Cocrystallization acyclovir-succinic acid using solvent evaporation methods", *Asian J. Pharm. Clin. Res.*, vol. 10, no. 6, pp. 91–94, 2017.
- [13] Dodd, W. James, Tonge, and H. Kenneth, *Thermal Methods*. Wiley India PVT., 2008.
- [14] F. Alatas, H. Ratih, and S. N. Soewandhi, "Enhancement of solubility and dissolution rate

- of telmisartan by telmisartan-oxalic acid co-crystal formation”, *Int. J. Pharm. Pharm. Sci.*, vol. 7, no. 3, pp. 423–426, 2015.
- [15] H. Yamashita, Y. Hirakura, M. Yuda, T. Teramura, and K. Terada, “Detection of cocrystal formation based on binary phase diagrams using thermal analysis.”, *Pharm. Res.*, vol. 30, no. 1, pp. 70–80, 2013.
- [16] N. I. Hilya, W. Agnes Nuniek, D. Setyawan, and E. Hendradi, “Improvement of dissolution properties through acyclovir - Succinic acid cocrystal using solvent evaporation technique”, *Int. J. Drug Deliv. Technol.*, vol. 7, no. 4, pp. 304–309, 2017.
- [17] F. Rahman, A. N. Winantari, D. Setyawan, and Siswandono, “Comparison study of grinding and slurry method on physicochemical characteristic of acyclovir – Succinic acid cocrystal”, *Asian J. Pharm. Clin. Res.*, vol. 10, no. 3, pp. 153–158, 2017.
- [18] K. Ma, Y. Zhang, H. Kan, L. Cheng, L. Luo, Q. SU, J. Gao, Y. Gao, J. Zhang, “Thermodynamic and Kinetic Investigation on the Crucial Factors Affecting Adefovir Dipivoxil-Saccharin Cocrystallization”, *Pharmaceutical Research*, vol. 31, pp. 1766-1778, 2014.



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Vol. 22 No. 3, April 2020

PREFACE

The development of materials science and technology plays an active role in the development of several fields of life including industry, medical, infrastructure, energy and the others. Researchers and academics are the forefront of this development and Indonesia Journal of Materials Science – JUSAMI – was founded to represent their needs, which are now widely recognized as an integral part of scientific and characterization investigations. JUSAMI Vol. 22 No. 3, April 2020 is proudly published several paper entitled: Magnetic Force Microscope Image Evaluation of Magnetic Iron Oxide Floppy Disc with Various Lift Height; Performance Study of LiBOB/LiTFSI Electrolyte Salt in the All-Solid-State Lithium-Ion Battery; Preparation of Acyclovir-Isonicotinamide Cocrystal by Solvent Evaporation Method with Methanol and Isopropanol; The Effect of Adsorbent Type and Ratio on Removal of Methylene Blue and Its Isotherm Adsorption; The Utilization of PET Waste as Raw Material for Producing Monofilament Yarn : The Effect of Winding Speed on the Physical and Mechanical Properties of the Yarn; Simulation of Iron Corrosion in Lead-Magnesium Eutectic (LME) Using Oxygen Inhibitor; and Effect of Crystallinity to Overpotential on Ni₃Fe Alloy As Electrocatalyst in Hydrogen Evolution Reaction.

All papers published in this volume of JUSAMI have been peer reviewed through processes administered by the journals Editors. Reviews were conducted by expert referees to the professional and scientific standards expected of a JUSAMI.

Finally, this issue would not have been possible without the greatest support of the Editorial Board and secretariat members, and we would like to express our sincere thanks to all of them. And all the Editorial Boards conveyed the support of the writers and reviewers, so that the Indonesia Journal of Material Science could display articles on quality research and development materials that are expected to contribute to the development of materials science.

Editor in Chief

Author Guidelines

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The topics discussed in Indonesian Journal of Materials Science are research & development results in: Material science and engineering; and Technological innovations and applications in industry based on materials such as polymers, ceramics, composites, metals or metal alloys, which are related to mechanical, magnetic, physical, dielectric or electronic properties with discussion includes: synthesis and modification and development of methods; testing and characterization; simulation and modeling; and nuclear engineering and its application in material science, etc.

2. Originality and novelty

The submitted text must be: own work/not the result of plagiarism; not rewriting without updates and novelty; and shows the current status supported by an adequate library

3. Systematic articles

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ARTICLE TITLE IS REWRITTEN IN UPPERCASE. Abstract is written in English include background, methodology, the results and conclusions. The abstract should be brief and clear, not exceeding than 200 words. Do not include art work, tables, elaborate equations or references.
- **Keywords**
maximum 5 words with the first word is the most important word.
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- **Experimental Method**
- **Materials and Instruments**
Includes an explanation of the material used in the study by stating the brand or origin of the material obtained, written in sentence form. For example, sodium chloride, pro analyst (Sigma-Aldrich), battery waste obtained from the Z plant. The equipment used in this paper mentioned the brand and type and its function in this experiment. For example Differential Scanning Calorimeter (DSC) Perkin Elmer Jade for thermal analysis, JEOL JEM 1400 Transmission Electron Microscope (TEM) for microstructure analysis.
- **Method and Procedure**
Method and Procedure is in the form of sentences that describe the steps of the research conducted.
- **Results and Discussion**
Discussion is carried out by referring to the objectives/hypotheses presented in INTRODUCTION and comparing with the results that already exist in the reference. At the end of the discussion, further research can be submitted. Tables are numbered and must be referred sequentially according to the contents of the article. Each table must be accompanied by a title and if there is a measurement result, the unit must also be written in the title section. Tables are made without vertical dividing lines. All images given numbers must be referenced in articles in sequence. Images are sent in the form of Excel files that can still be edited for graphics and in the form of bitmaps (BMP, JPEG, TIFF, GIF) for photos/images. Images in the form of bitmaps must have a resolution of more than 300 dpi, unless there is a resolution limit for scientific reasons. Labels/captions are given in separate parts of the image. Graphs are given names and units on the axis. The writing of chemical equations and or mathematical agreements is carried out by the Microsoft Equation program and is numbered with Arabic numbers according to the discussion flow. Abbreviations must be completed at the beginning of loading in the article.
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Manuscripts must include data with provisions including:

- The amount of data presented can be considered sufficient.
- Data is presented in graph/table form and has been given sufficient information
- Data presented has been accompanied by discussion.

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