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PREFACE From Chairman

It is our pleasure to present you the proceedings of The 1st International Conference on Pharmaceutics and Pharmaceutical Sciences (ICPPS) organized by The Faculty of Pharmacy Universitas Airlangga Surabaya Indonesia.

The proceeding was produced based on papers and posters presented at The 1st International Conference on Pharmaceutics and Pharmaceutical Sciences (ICPPS), held in Surabaya, Indonesia, 14-15 November 2014.

The proceeding clearly reflects broad interest, from the participants that coming from all around the world.

The papers presented were pharmaceutics and biopharmaceutics; requirements on how to evaluate molecules in discovery and their appropriateness for selection as potential candidate; their development in context of challenges and benefits, together with associated time and cost implications and also requirements to progress through pre-clinical and clinical.

In this an opportunity, I would like to express my appreciation to the editorial team of the proceeding who have been working hard to review manuscripts, and making the first edition of this proceeding be possible.

I would like also to thanks to all invited speakers and presenters who participated in The 1st International Conference on Pharmaceutics and Pharmaceutical Sciences (ICPPS) and your contribution to this proceeding.

Finally, I hope this proceeding will give contribution to the Pharmaceutics and Pharmaceutical Sciences research.

Chairman,

Dra. Esti Hendradi, MSi., Ph.D., Apt
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MOLECULAR MODELING AND SYNTHESIS OF 1-(3,4-DICHLOROGENZOLYL)-1,3-DIMETHYLUREA

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INTRODUCTION
Cancer is a top killer of human beings. There is an urgency to develop highly efficacious and minimally toxic treatments for cancer. Most of the current cancer drugs usually exhibit high toxicity and are severely resisted by tumor cells in the clinic. This dilemma is particularly true for DNA-damaging agents, the mainstay of cancer treatment (Tao et al, 2007). Following DNA damage, normal cells arrest and attempt to repair at the cell cycle checkpoints G1 and S phases through tumor suppressor p53, and at G2 and S phases through checkpoint 1 kinase (Chk1) (Zhao et al, 2010). Checkpoint Kinase-1 (Chk1, CHK1, CHEK1) is a Ser/Thr protein kinase that mediates the cellular response to DNA-damage. Upon DNA-damage, Chk1 is activated by ATM and ATR kinases, which phosphorylate residues Ser-317 and/or Ser-345. Chk1 mediated signalling ultimately leads to S-phase or G2/M cell cycle arrest primarily driven by Cdk inhibition. Consequently Chk1 inhibition would abrogate this arrest, and therefore permit a cell with damaged DNA to continue through the cell cycle, ultimately resulting in mitotic catastrophe and/or apoptosis (Oza et al, 2006). Thus, selective inhibitors of Chk1 may be of great therapeutic value in cancer treatment (Li et al, 2006).

Several studies have been developed on urea derivatives as Chk1 inhibitors. As a part of our research for novel anticancer agents, we designed and synthesized 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea. Docking simulation was performed using Molegro Virtual Docker of the Chk1 in complex with an inhibitor to explore the binding modes of this compound at the active site.

MATERIAL AND METHODS
Materials and Measurements
All chemicals and reagents used in current study were analytical grade. The IR spectra was recorded on FT-IR Perkin Elmer Spectrum One. The 1H-NMR and 13C-NMR spectra were recorded on BRUKER BioSpin Avance III NMR Spectrometer in Chloroform-d6 and chemical shift was reported in ppm (δ).

General Procedure for Synthesis of 1-(3,4-Dichlorobenzoyl)-1,3-Dimethylurea
To a stirred solution of 1,3-dimethylurea (0.08 mol) and triethylamine (0.08 mol) in THF (30 mL) was added 3,4-dichlorobenzoyl chloride (0.04 mol) in THF (15 mL) and the reaction mixture was reflux for 4 hour. The product was washed carefully with water and extracted with ethyl acetate; the resulting 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea was purified by crystallization from EtOH (Figure 1).

Molecular Modeling
To assess the anti-cancer behavior of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea on structural basis, automated docking studies were carried out using Molegro Virtual Docker program, the scoring functions and hydrogen bonds formed with the surrounding amino acids are used to predict their binding modes, their binding affinities and orientation of this compound at the active site of the Chk-1 enzyme. The protein-ligand complex was constructed based on the X-ray structure of Chk-1 (2YWP.pdb downloaded from the pdb).

RESULT AND DISCUSSION
Chemistry
In our study, 1,3-dimethylurea and 3,4-dichlorobenzoyl chloride were dissolved in a mixture of TEA and THF, then refluxed for 4 h at 80°C, and white needle crystal of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea was obtained with yields of 75% and melting point 110°C. The synthetic compound gave satisfactory analytical and spectroscopic data, which was in full accordance with their depicted structures.

![Chemical structure](image1)

Figure 1. Synthetic scheme for 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea

The IR spectrum of the synthesized urea was recorded (Figure 2) and it gives an absorption band 3316 cm⁻¹ representing the presence of -NH group. The absorption band at 1696 and 1652 cm⁻¹ confirms the imide group, and the absorption band at 1534 cm⁻¹ confirms the aromatic -C=O- group.

![IR spectra](image2)

Figure 2. IR spectra of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea in KBr

The 1H-NMR spectra (Figure 3) of synthesized urea give 1H-NMR (400 MHz, Chloroform-d6, δ ppm): 2.89 (d, 3H), 3.15 (s, 3H), 7.21-7.52 (m, 3H), 8.83 (s, 1H). The 13C-NMR spectra (Figure 4) of synthesized urea give 13C-NMR (400 MHz, Chloroform-d6, δ ppm): 27.22 (-CH3), 35.75 (-CH3), 125.93-135.74 (-Ph), 155.79 (-C=O), 173.53 (-C=O).

![NMR spectra](image3)

Figure 3. 1H-NMR spectra of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea in Chloroform-d6

![NMR spectra](image4)

Figure 4. 13C-NMR spectra of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea in Chloroform-d6

**Molecular Modeling**

In order to gain more understanding of the activity observed at the Chk1, molecular docking of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea into ATP binding site of Chk1 was performed on the binding model based on the Chk1 complex structure (2YWP.pdb). The binding model of this compound and Chk1 is depicted in Figure 5. 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea shows Rerank Score of -68,1456 and form one hydrogen bond between carbonyl moiety and Cys 87.
CONCLUSION

A novel 1-benzoyl-1,3-dimethylurea has been designed and synthesized. The white needle crystal of 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea was obtained with yields of 75% and melting point 110°C. The synthetic compound gave satisfactory analytical and spectroscopic data, which was in full accordance with their depicted structures. Docking simulation was performed to position the compound into the Chk1 active site to determine the probable binding model. 1-(3,4-dichlorobenzoyl)-1,3-dimethylurea shows Rerank Score of -68,1456 and form one hydrogen bond between carboxyl moiety and Cys 87.

REFERENCES


* Tao, Z., Li, G., Tong, Y., Stewart, K., et al. (2007). Discovery of 4’-(1,4-di hydro-indeno[1,2-c]pyrazol-3-yl) benzonitriles and 4’-(1,4-dihydroindeno[1,2-c]pyrazol-3-yl) pyridine-2’-carbonitriles as potent checkpoint kinase 1 (Chk1) inhibitors. Bioorg Med Chem Lett. 17: 5944–5951