



Molecular Docking of Benzoylurea Derivatives as Potential Anti-Breast Cancer Agent and Its Admet Profiles

Aguslina Kirtishanti^{1,2}, Siswandono^{2*}, Suko Hardjono², Dini Kesuma³

1. Department of Clinical and Community Pharmacy, Faculty of Pharmacy, University of Surabaya, Kalirungkut, Surabaya 60293, East Java, Indonesia.
2. Department of Medicinal Chemistry, Faculty of Pharmacy, University of Airlangga, Airlangga No. 4-6, Surabaya 60115, East Java, Indonesia.
3. Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Surabaya, Kalirungkut, Surabaya 60293, East Java, Indonesia.

*Corresponding Author: Siswandono

Abstract

Objective: At present therapy for breast cancer leads to target cell therapy. One of the compounds that can be developed as anti-breast cancer agents is benzoylurea. Benzoylurea has the same pharmacophore group with hydroxyurea as urea derivatives which have anticancer activity. This study aims to predict the anticancer activity and ADMET profile of seven benzoylurea-derived compounds as candidates cytotoxic agent for breast cancer. **Method:** Biological activity of benzoylurea derivatives is predicted through molecular modeling (in silico) using the Autodock program, ADME profiles and toxicity can be predicted using the pkCSM program and the Protox II online tool. In silico test was carried out by docking between benzoylurea derivatives and HER2 receptor targets, PDB ID. 3PP0. **Result:** All benzoylurea-derived compounds studied were compliant with Lipinski's 5 legal requirements. The 4-tert-butylbenzoylurea compound shows a better ADME profile and its toxicity is predicted to have mutagenic properties but not hepatotoxic properties. The smallest docking score of seven benzoylurea derivatives is 4-tert-butylbenzoylurea, therefore the compound has the best cytotoxic activity. **Conclusion:** the 4-tert-butylbenzoylurea compound is chosen as the compound to be synthesized and further developed.

Keywords: *Molecular docking; Benzoylurea; Anti-breast cancer; ADMET profiles.*

Introduction

Cancer that is frightening for women in the world is breast cancer which is the second most common cancer in the world. The prevalence of breast cancer with new cases in 2018 is 24.2% in women spread across 154 countries and breast cancer deaths by 15% [1]. Efforts to develop anticancer drugs are still being made to overcome drugs that are not selective against cancer cells and also to drugs that have experienced resistance.

Efforts to develop existing drugs can be made by designing drugs that aim to get new drugs with the desired biological effects and reduce the side effects that exist through structural modification. Structural modification is carried out by synthesizing several derivatives of the guiding compound, identifying the structure and testing its

biological activity [2]. Before a compound is synthesized, a method is needed to predict the physicochemical properties of a drug molecule, its pharmacokinetic profile and toxicity and its interactions with the receptor. The method for predicting the molecular properties of drugs is called molecular modeling or in silico [3].

In silico technique is done through a simulation of drug-receptor interaction process or called docking with the help of computers [4]. Docking is an attempt to align the ligand as a small molecule into the target cell, which is a large protein molecule [5]. The development of anticancer drugs is currently aimed at targeting cancer cells. The class of anticancer drugs that have a mechanism of action on target cells is the

tyrosine-kinase inhibitor group. Tyrosine kinase receptors are a group of erbB receptors that play a key role in the signal transduction pathway by regulating cell division and differentiation.

Under certain conditions such as excessive receptor expression and mutations, these receptors can become hyperactive, causing uncontrolled cell proliferation [6,7,8]. Among the tyrosine kinase receptors that have been identified as important in breast cancer are the human epidermal growth factor receptor (HER-2 or erbB-2). Deregulation of growth signals due to hyperactivation of the HER-2 receptor is seen in breast cancer [9].

About 20% -30% of breast cancer patients is overexpressed with HER2, resulting in intracellular signaling irregularities that correlate with aggressive tumour growth and poor clinical prognosis [10]. Some benzoylurea-derived compounds show good cytotoxic activity compared to hydroxyurea using the Brine Shrimp Lethality Test (BST) method [11].

Cytotoxic activity tests were also carried out on compounds 1- (4-trifluoromethyl-benzoyl) -3-benzoylurea using MCF7 cells and gave results that the compounds could be used as anticancer agents [12]. In this study, an in silico test was performed on seven benzoylurea-derived compounds using the Autodock Tools 4.2.6 program to predict its anticancer activity.

The in silico test is done through docking with the HER2 receptor using the PDB code: 3PP0, the original ligand is SYR127063 [13]. The docking results were compared with hydroxyurea as a drug compound containing urea and lapatinib as a drug used clinically. In silico test results in the form of bond energy values or docking scores.

The smaller the docking score indicates the more stable the drug-receptor binding so that can be improved the anticancer activity. After the in silico test, the prediction of pharmacokinetic profiles (ADME) and toxicity was performed using the pkCSM program and the Protox II online tool. Benzoylurea-derived compounds that have the greatest anticancer activity will be selected for further synthesis based on the docking score and ADMET profile.

Materials and Methods

Programs

Chem Bio Draw Version 15 (CambridgeSoft), a licensed software; Chem Bio 3D Version 15 (CambridgeSoft), a licensed software; Marvin Sketch and Avogadro software; Autodock Tools 4.2.6; SMILES Translator; pkCSM dan Protox II online tool is free online tool.

Receptor

The molecular structure of receptor HER2 can be downloaded via the protein data bank site. In this study, HER2 receptor with PDB ID: 3PP0 was selected as a target protein, because it contains a ligand 2-{2-[4-(5-chloro-6-[3 (trifluoromethyl)phenoxy]pyridin-3-yl)amino)-5Hpyrrolo [3,2-d]pyrimidin-5yl]ethoxy}-ethanol (SYR127063) [13].

Ligand

The structure of benzoylurea derivatives and comparison compounds, hydroxyurea (HU) and lapatinib, were drawn 2-D molecular structures using Marvin Sketch programme and then copied into Avogadro to make the structure 3-D. The structure of the ligand in the 3-D form is stored as *Mol2 file [2].

Molecular Docking

The ligands in the 3-D form are docking with HER2 receptors (3PP0) using Autodock Tools. The results obtained in the form of a docking score are the energy needed in the ligand-receptor interaction process. From the docking score, it can be predicted the anticancer activity of compounds through HER2 signaling inhibition [2].

Prediction of Admet of Compounds

Prediction of physicochemical properties such as molecular weight (BM), logarithm of octanol / water partition coefficient (log P), number of bonds between atoms that can rotate (Torsion); Hydrogen Bond Acceptors (HBA), Hydrogen Bond Donors (HBD), Polar Surface Activity (PSA) and pharmacokinetic profiles (ADME) and the toxicity of benzoylurea-derived compounds were carried out using pkCSM and Protox II online tools [15]. Before docking, seven benzoylurea derivatives and comparison compounds (hydroxyurea and lapatinib) were drawn 2-D molecular structure with Chem-Bio Draw Ultra Version 15 program, then copied in the Chem-Bio 3D Ultra Version 15 program to make 3-D structures, then stored as *SD file or *PDB file.

Compounds in the 3-D structure are translated into the SMILES format using the Online SMILES Translator [14]. Furthermore, the compound in the form of SMILES format is processed using pkCSM online tool [15] to predict the ADME and the toxicity of the compounds. Prediction of oral toxicity (LD50) in rodents and the classification of compound toxicity based on

the Globally Harmonized System (GHS) using the Protox II online tool [16, 17].

Results and Discussion

The chemical structure of benzoylurea derivatives and comparative compounds, hydroxyurea (HU) and lapatinib, can be seen in Figure 1 and Table 1.

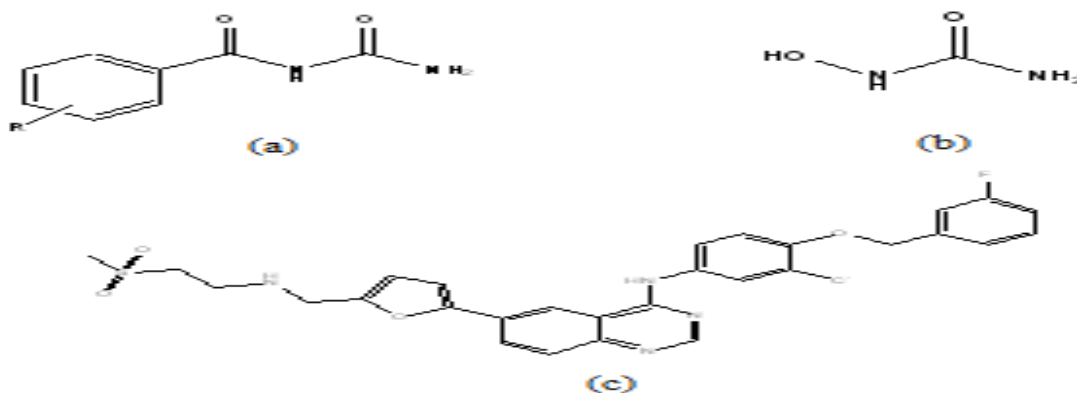


Fig. 1: Benzoylurea derivatives (a), Hydroxyurea (b), and Lapatinib (c)

Table 1: Chemical structure of benzoylurea-derived compounds

| Compound Code | Position | R | Name of Compound |
|---------------|----------------------|----------------------------------|------------------------------|
| BU-1 | 4 | H | benzoylurea |
| BU-2 | 4 | OCH ₃ | 4-methoxybenzoylurea |
| BU-3 | 4 | C(CH ₃) ₃ | 4-tertbutylbenzoylurea |
| BU-4 | 4 | CF ₃ | 4-trifluoromethylbenzoylurea |
| BU-5 | 2 | Cl | 2-chloro benzoylurea |
| BU-6 | 4 | Br | 4-bromo benzoylurea |
| BU-7 | 4 | NO ₂ | 4-nitro benzoylurea |
| HU | Comparative compound | | Hydroxyurea |
| Lapa | Comparative compound | | Lapatinib |

Prediction of Physicochemical Properties and ADMET Profile

Lipinski analyzed 2,245 drugs from World Drugs Index data and concluded that the compound would be difficult to absorb and the permeability would be low if it had: a molecular weight higher than 500, a log value of the octanol / water partition coefficient (log P) higher than +5; donor H-bonds (HBD) expressed by the number of O-

H and N-H groups, greater than 5; and the H-acceptor (HBA) bond expressed by the number of O and N atoms is greater than 10. The analysis is known as the Lipinski law of five because all values are multiples of the number five [18]. In silico prediction of the physicochemical properties of the benzoylurea-derivatives can be seen in table 2, and the ADMET profile is shown in Table 3.

Table 2: Prediction of in silico values of physicochemical properties of benzoylurea derivatives and comparison compounds using pkCSM online tool.

| Compound Code | BM | Log P | HBA | HBD | Torsion | PSA (Å ²) | Legal Requirements 5 Lipinski |
|---------------|---------|--------|-----|-----|---------|-----------------------|-------------------------------|
| BU-1 | 164,164 | 0,4951 | 2 | 2 | 1 | 69,374 | Yes |
| BU-2 | 194,19 | 0,5037 | 3 | 2 | 2 | 80,853 | Yes |
| BU-3 | 220,272 | 1,7926 | 2 | 2 | 1 | 94,834 | Yes |
| BU-4 | 232,161 | 1,5139 | 2 | 2 | 1 | 88,236 | Yes |
| BU-5 | 198,609 | 1,1485 | 2 | 2 | 1 | 79,677 | Yes |
| BU-6 | 243,06 | 1,2576 | 2 | 2 | 1 | 83,242 | Yes |

| | | | | | | | |
|------|---------|---------|---|---|----|---------|-----|
| BU-7 | 209,161 | 0,4033 | 4 | 2 | 2 | 84,027 | Yes |
| HU | 76,056 | -0,9561 | 2 | 3 | 0 | 28,539 | Yes |
| Lapa | 581,069 | 6,1391 | 8 | 2 | 11 | 235,650 | Yes |

BM = molecular weight; LogP = logarithm of octanol/water partition coefficient; Torsion = bond between rotating atoms (rotatable bond); HBA = hydrogen bond acceptors; HBD = hydrogen bond donors; PSA = polar surface activity

Based on table 2, it can be seen that the molecular weight of benzoylurea derivatives has a range of 164.164 to 243.06 (<500), log P values in the range 0.4033 - 1.7926 (<5), the number of HBD with a value of 2 (<5), and

the number of HBAs in the range 2-4 (<10). These results indicate that all the benzoylurea derivatives studied were compliant with Lipinski's legal requirements [18].

Table 3: ADMET profile of benzoylurea derivatives using pkCSM and Protox online tools.

| Compound Code | Absorption | | | Distribution | | | Metabolism | | Excitation | Toxicity | | | |
|---------------|--------------------|--------------------------|----------------------------|--------------|------------------|------------------|------------------|------------------|-----------------------------|---------------|----------------|--------------------------|-------|
| | Intestinal abs (%) | Skin Permeability (cm/h) | Caco-2 Permeability (cm/s) | VDs | BBB Permeability | CNS Permeability | CYP2D6 Inhibitor | CYP3A4 Inhibitor | Total Clearance (ml/min/kg) | Ames Toxicity | Hepatotoxicity | LD ₅₀ (mg/kg) | Class |
| BU-1 | 65,745 | -3,155 | 0,016 | -0,4 | 0,074 | -2,927 | No | No | 0,378 | No | No | 818 | 4 |
| BU-2 | 85,598 | -3,224 | 0,382 | -0,311 | 0,243 | -2,685 | No | No | 0,617 | No | No | 2000 | 4 |
| BU-3 | 92,819 | -2,852 | 0,895 | 0,019 | 0,014 | -2,174 | No | No | 0,236 | Yes | No | 1950 | 4 |
| BU-4 | 88,86 | -3,314 | 0,062 | -0,544 | 0,395 | -2,954 | No | No | 0,136 | No | Yes | 3000 | 5 |
| BU-5 | 69,722 | -3,247 | 0,023 | -0,376 | 0,108 | -2,933 | No | No | 0,087 | No | No | 1950 | 4 |
| BU-6 | 69,94 | -3,254 | 0,029 | -0,378 | 0,152 | -2,931 | No | No | 0,207 | No | No | 1950 | 4 |
| BU-7 | 73,573 | -2,791 | 0,081 | -0,563 | 0,549 | -2,701 | No | No | 0,67 | Yes | No | 570 | 4 |
| HU | 73,127 | -4,319 | 0,494 | -0,495 | 0,545 | -3,488 | No | No | 0,659 | Yes | No | 5760 | 6 |
| Lapa | 97,254 | -2,735 | 0,098 | 0,083 | 1,076 | -3,153 | No | Yes | 0,565 | No | Yes | 1500 | 4 |

The compound is said to have excellent absorption if the value of intestinal absorption is above 30% [19]. It can be seen in Table 3 that benzoylurea-derived compounds have proper intestinal absorption, and the highest intestinal absorption value is BU-3 compound. HU has lower intestinal absorption value than BU-3 while lapatinib has a slightly higher absorption value than BU-3. Skin permeability is an essential consideration for the development of transdermal drugs. To predict whether a compound can penetrate the skin, it can use

a skin permeability constant that is log Kp (cm/h). If the log Kp > -2.5 means that the compound has a relatively low penetration in the skin [19].

Based on table 3, benzoylurea-derived compounds have log Kp in the range of -2.791 to -3.314 cm/h (<-2.5), therefore it can be said that benzoylurea-derived compounds have good penetration into the skin. Likewise, HU and lapatinib as comparison compounds have good penetration into the skin. Caco-2 is a cell line derived from human colorectal

adenocarcinoma epithelial cells. This cell is used extensively as an in vitro model of human intestinal mucosa to predict absorption of drugs given orally. The compound that is predicted to have a high Caco-2 permeability if it has a log Papp value > 0.90 cm / s [19]. From table 3, it is known that all benzoylurea-derived compounds and comparison compounds have low Caco-2 permeability.

Among the seven benzoylurea-derived compounds, compounds with BU-3 codes have log Papp of 0.895 (close to 0.9). Volume distribution (VDss) is the volume required for a drug dose to be homogeneously distributed at a balanced level in blood plasma. The higher the distribution volume, the more drugs are distributed in the tissue than in the plasma.

Based on the pkCSM prediction, that the distribution volume (VDss) is low if the log VDss < -0.15 and the distribution volume is high if the log VDss > 0.45 [19]. All of the benzoylurea-derived compounds, only compounds with BU-3 code (4-tert-butylbenzoylurea) can be distributed equally in blood plasma, as well as lapatinib as comparison compound.

The ability of drugs to penetrate the brain through the blood-brain barrier (BBB) is an important parameter to reduce side effects and toxicity or to improve the pharmacological activity of drugs in the brain. BBB permeability is measured in vivo in animal models as log BB. If the log BB > 0.3 is said to be the compound can penetrate the blood-brain barrier directly, but the compound with log BB < -1 means that it is poorly distributed into the brain [19].

In addition to BBB permeability, CNS (Central Nervous System) permeability is also essential, namely the ability of drugs to be able to penetrate the CNS. Log PS expresses CNS permeability if compounds with log PS > -2 are considered to be able to penetrate the CNS, whereas compounds with log PS < -3 are predicted not to be penetrated CNS [19].

It can be seen in Table 3 that all benzoylurea-derived compounds are predicted to penetrate moderately into BBB and CNS. HU as a comparative compound is predicted to be moderately penetrated into

BBB but not penetrated into CNS, whereas lapatinib can not penetrate either into the BBB or CNS.

Cytochrome P450 is an enzyme that is responsible for the metabolism of many drugs. Inhibitors of these enzymes can change the pharmacokinetics of these drugs, so it is critical to evaluate whether a compound can affect cytochrome P450. There are two main isoforms responsible for metabolism, namely 2D6 (CYP2D6) and 3A4 (CYP3A4) [19].

From table 3, it can be seen that all benzoylurea-derived compounds do not affect or inhibit CYP2D6 and CYP3A4. HU also does not affect both the enzymes except lapatinib can affect the CYP3A4 enzyme. Drug clearance is measured by the proportionality constant CLtot and occurs primarily as a combination of hepatic clearance and renal clearance.

The higher the CLtot value of the compound, the faster the excretion process [19]. Based on table 3, the CLtot of benzoylurea-derived compounds is in the range of -0.207 to 0.67 ml/min/kg. The CLtot values state that the speed of excretion of benzoylurea-derived compounds can be predicted. To determine the toxicity of compounds, the Ames Toxicity test and hepatotoxicity test can be done. Ames Toxicity is a method used to assess the potential for mutagenic compounds using bacteria.

The test results stated positive means showing the compound is mutagenic and can be carcinogenic [19]. The compound that showed at least one pathological or physiological hepatic event was considered hepatotoxic and highly related to liver disruption [20]. From table 3 it can be seen that compounds with BU-3 and BU-7 codes, 4-tert-butylbenzoylurea and 4-nitrobenzoylurea are positive in the Ames Toxicity test, whereas compounds with BU-4 code (3-trifluoro methylbenzoylurea) are predicted to be hepatotoxic.

HU is also positive in the Ames Toxicity test and lapatinib is positive in hepatotoxicity. The lethal dose (LD50) is the number of compounds administered which can cause the death of 50% of experimental animals. LD50 is a standard measurement of acute toxicity

that is used to assess the relative toxicity of a different compound.

To determine the prediction of the toxicity of benzoylurea derivatives, an acute oral toxicity test for rodent (LD50) and acute toxicity classification of compounds based on Globally Harmonized System (GSH) using the Protox II online tool.

Based on table 3, it can be seen that benzoylurea derivatives are predicted to have LD50 values ranging between 570 - 3000 mg/kg and are included in the toxicity class 4 and 5 based on GHS. There are six benzoylurea-derived compounds namely BU-1 to BU-3 and BU-5 to BU-7 which belong to the 4 GSH toxicity class ($300 < LD50 \leq 2000$) with the indication "harmful if swallowed", this means that the compound is predicted to be of a slightly toxic. One benzoylurea-

derived compound, BU-4 which belongs to class 5 GSH ($2000 < LD50 \leq 5000$) with an indication "may be harmful if swallowed", this means that the compound is predicted to have relatively low acute toxicity. Lapatinib is included in the toxicity class 4 according to GSH, this means that lapatinib is a slightly toxic compound. HU is predicted as non toxic compound according GSH classification.

Molecular Docking

Molecular docking is done to determine the pharmacological activity of benzoylurea derivatives and to explain the interaction between ligands and receptors. The docking results of benzoylurea derivatives and comparative compounds with HER2 receptor targets (PDB code: 3PP0) and its interaction with amino acids target on HER2 receptor can be seen in Table 4 and 5.

Table 4: Docking score of benzoylurea derivates and comparative compounds by docking with Autodock Tools

| Compound Code | Docking Score |
|---------------|---------------|
| BU-1 | -5,88 |
| BU-2 | -5,88 |
| BU-3 | -7,01 |
| BU-4 | -6,02 |
| BU-5 | -6,42 |
| BU-6 | -6,55 |
| BU-7 | -6,42 |
| HU | -3,02 |
| Lapa | -10,80 |

From table 4, the compound that has the smallest docking score is a BU-3 compound. This shows that BU-3 compound is predicted to has the best anticancer activity among benzoylurea derivatives. The smaller the docking score indicates that the ligand-receptor bond is more stable.

Anticancer activity of benzoylurea-derived compounds is predicted to be still lower compared to lapatinib.

When the benzoylurea-derived compounds are compared with hydroxyurea, the anticancer activity of benzoylurea derivatives is predicted to be better.

Based on table 5, BU-3 compound has the most number of hydrogen bonds among the benzoylurea derivatives. The hydrogen bonds are strengthened by the steric interactions on

Val 734, Lys 753 and Leu 796 which cause BU-3 compound to has the smallest docking score. HU has 5 hydrogen bonds and 1 steric interaction while lapatinib has 4 hydrogen bonds and is strengthened with many steric interactions which causes the predicted anticancer activity of lapatinib to be better than benzoylurea derivatives.

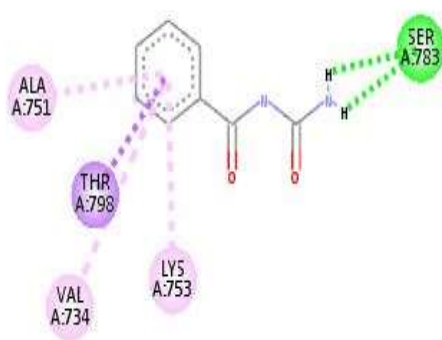
However,there are many cases found that lapatinib has resistance [21, 22] so it is necessary to develop new drugs that can overcome the deficiencies of lapatinib and are selective against cancer cells.

2D View of the interaction of the benzoylurea derivates and comparative compounds with HER2 receptor targets can be seen in Figures 2 and 3. Amino acids receptor targets HER2 involved in interactions with benzoylurea derivatives and comparative compounds can be seen in Table 5.

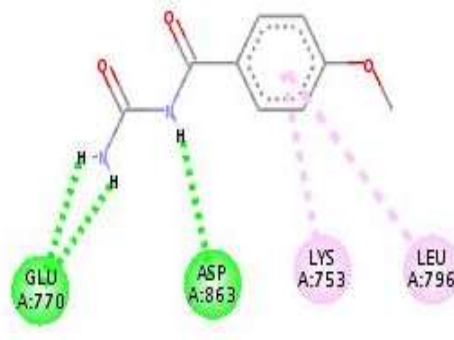
Table 5: Interaction of benzoylurea derivatives and comparative compounds with amino acids on HER2 receptor

| Compound Code | Hydrogen Bond and Steric Interactions | | | | | | | | | | | | | | | | | | | | |
|---------------|---------------------------------------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| | Ser 783 | Ser 782 | Asp 786 | Asn 785 | Thr 786 | Arg 784 | Glu 770 | Gln 779 | Ala 751 | Val 734 | Lys 753 | Thr 779 | Leu 796 | Lys 753 | Leu 785 | Met 801 | Met 774 | Phe 864 | Leu 785 | Leu 726 | Cys 780 |
| BU-1 | 2 H | - | - | - | - | - | - | - | 1 S | 1 S | 1 S | 1 S | | | | | | | | | |
| BU-2 | | | 1 H | | | | 2 H | | | | 1 S | | 1 S | | | | | | | | |
| BU-3 | - | 2 H | 1 H | 1 H | 1 H | - | - | - | 1 S | 2 S | | 1 S | | | | | | | | | |
| BU-4 | | | 1 H | | | | 2 H | | 2 S | 1 S | 1 H | 2 S | | 2 S | | | | | | | |
| BU-5 | 2 H | | 1 S | | 1 H | | | | 1 S | 2 S | 2 S | 1 S | | | | | | | | | |
| BU-6 | | | 1 H | | | | 2 H | | 1 S | 1 S | 1 H | 1 S | | 1 S | | | | | | | |
| BU-7 | | | 1 H | | 1 H | | 2 H | | | | 1 S | | | | | | | | | | |
| HU | - | 1 H | 1 H | 1 H | - | 2 H | | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Lapa | - | 1 H | - | - | 1 H | - | | 2 H | 2 S | 1 S | | | 2 S | 2 S | 1 S | 1 S | 1 S | 1 S | 1 S | 2 S | 1 S |

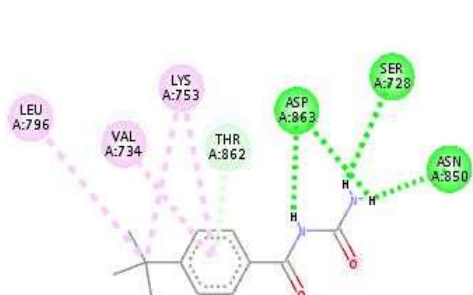
H:hydrogen bond; S:Steric Interactions (Van der Waals and Hydrophobic Bonds)



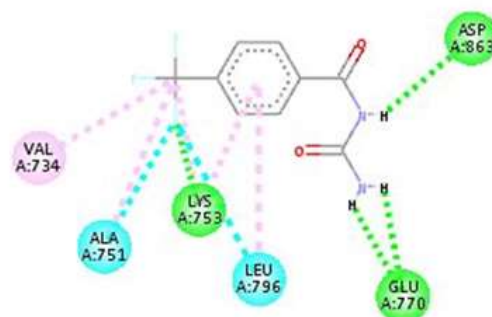
(a)



(b)



(c)



(d)

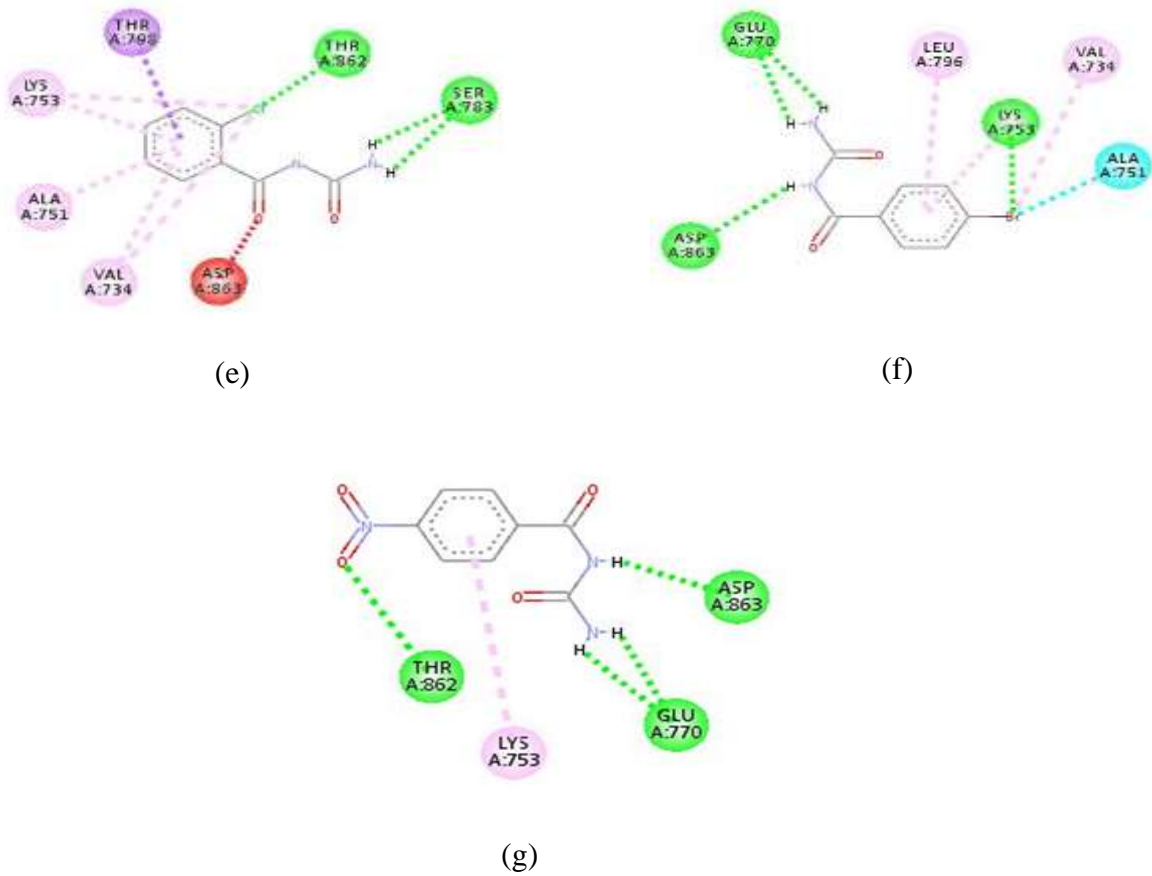


Fig. 2: The binding mode 2D view of the benzoylurea derivates with HER2 receptor targets: BU-1(benzoylurea)(a); BU-2 (4-methoxybenzoylurea)(b); BU-3(4-tertier butylbenzoylurea) (c); BU-4(4-trifluoro methylbenzoylurea) (d); BU-5 (2-chloro benzoylurea) (e); BU-6 (4-bromo benzoylurea) (f); BU-7 (4-nitro benzoylurea) (g)

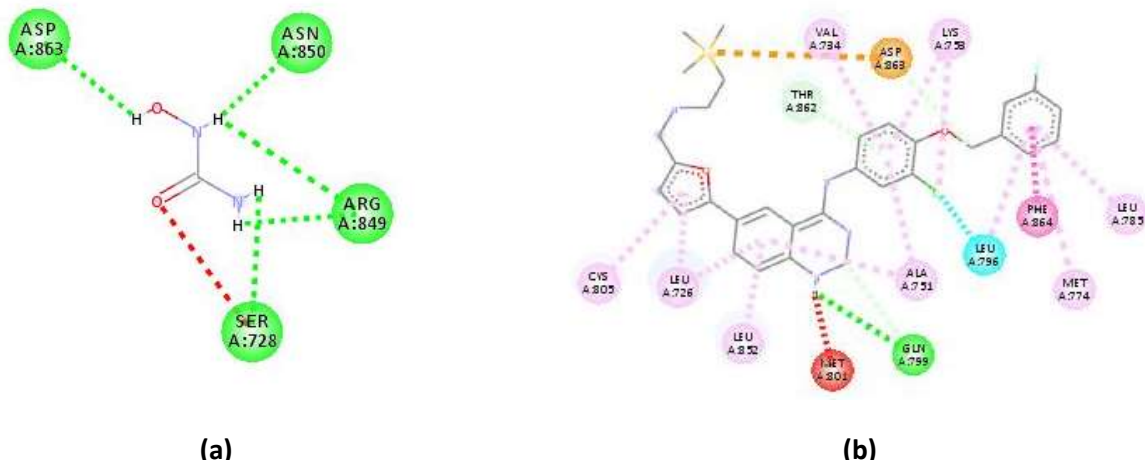


Fig. 3: The binding mode 2D view of the comparative compounds with HER2 receptor targets: HU (Hydroxyurea) (a); Lapatinib(b)

Conclusion

From the results of research on molecular docking and ADMET profiles, it can be concluded that the BU-3 compound (4-tertier butylbenzoylurea) is the compound selected

for further synthesis and in vitro testing of anticancer activity on breast cancer cells.

Acknowledgements

This research was financially supported by DRPM DIKTI 2019

References

- International Agency for Research on Cancer (2019) World Health Organization. <https://www.who.int/cancer/PRGlobocanFinal.pdf> 2018; 2-3: 18.
- Siswandono (2016) Medicinal Chemistry I. 2nd ed. Surabaya: Airlangga University Press.
- Schlick T (2010) Molecular Modeling and Simulation : An Interdisciplinary Guide. 2nd ed. New York: Springer Science+Business Media.
- Hinchliffe A (2008) Molecular Modeling for Beginners. 2nd ed. Chichester: John Wiley and Sons Ltd.
- Jensen F (2007) Introduction to Computational Chemistry. 2nd ed. Chichester: John Wiley & Sons Ltd, 415-416.
- Singh M, Jadhav HR (2017) Targeting non-small cell lung cancer with small-molecule EGFR tyrosine kinase inhibitors. Drug Discovery Today, doi: <https://doi.org/10.1016/j.drudis.2017.10.004>.
- Zulkifli AA, Tan FH, Putoczki TL, Stylli SS, Luwor RB (2017) STAT3 signaling mediates tumour resistance to EGFR targeted therapeutics. Molecular and Cellular Endocrinology, 451:15-23.
- Alanazi IO, Khan Z (2016) Understanding EGFR Signaling in Breast Cancer and Breast Cancer Stem Cells: Overexpression and Therapeutic Implications. Asian Pac. J. Cancer Prev., 17(2): 445-453.
- Li HQ, Yan T, Yang Y, Shi L, Zhou CF, Zhu HL (2010) Synthesis and structure-activity relationships of N-benzyl-N-(X-2-hydroxybenzyl)-N'-phenylureas and thioureas as antitumor agents. Bioorganic & Medicinal Chemistry, 18(2010):305-313.
- Hawthorne VS, Huang WC, Neal CL, Tseng LM, Hung MC, Yu D (2009) ErbB2-mediated Src and STAT3 Activation Leads to Transcriptional Upregulation of p21^{Cip1} and Chemoresistance in Breast Cancer Cells. Mol. Cancer Res, 7(4): 592-600.
- Diyah NW, Siswandono, Hardjono S, Purwanto BT (2013) Molecular Modeling and Quantitative Relationship of Structure-Cytotoxic Activity of Benzoilurea Derived as Antitumor. Berkala Ilmiah Kimia Farmasi, 2(2): 20-27.
- Suhud F, Siswandono, Budiati T (2017) Synthesis and Activity Test of 1-Benzyl-3-benzoylurea Compounds with Bromo, Kloro, Floro and Triflorometil substitution in para position as Antiproliferative Agent. Media Pharmaceutica Indonesiana, 1(3):154-163.
- Aertgeerts K, Skene R, Yano J, Sang BC, Zou H, Snell G, et al (2011) Structural Analysis of The Mechanism of Inhibition and Allosteric Activation of the Kinase Domain of HER2 Protein. J. Biol. Chem., 286(21):18756-18765.
- National Cancer Institute (2019) Online SMILES Translator. United States <https://cactus.nci.nih.gov/translate/> 18.
- Pires DEV, Blundell TL, Ascher DB (2019) The University of Melbourne's pkCSM Small-molecule Pharmacokinetics Prediction. <http://biosig.unimelb.edu.au/pkcsm/prediction/> 18.
- Charite University of Medicine-Institute for Physiology (2019) ProTox-II-Prediction of Toxicity of Chemicals. http://tox.charite.de/protox_II/ 18.
- Kesuma D, Siswandono, Purwanto BT, Hardjono S (2018) Cytotoxic Activity and Toxicity in silico of N-(Benzoyl)-N'-phenyltiourea Derived Compounds as Anticancer Drug Candidates. J. Pharm. Sci. Clin Res., 3(1):1-11.
- Lipinski CA, Lombardo F, Dominy BW, Feeney PJ (1997) Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings. Adv. Drug Deliv. Rev., 23(1-3):3-26.
- Pires DE, Blundell TL, Ascher DB (2015) pkCSM: Predicting Small Molecule Pharmacokinetic and Toxicity Properties using Graph-based Signatures. J. Med. Chem., 58(9):4066-4072. DOI:10.26434/chemrxiv-2015-5b00104.
- Ekowati J, Diyah NW, Novianti KA, Hamid IS, Siswandono (2018) Molecular Docking of Ferulic Acid Derivates on P2Y12 Receptor and their ADMET Prediction. J. Math. Fund. Sci., 50(2):203-219.

21. Yallowitz A, Garcia L, Alexandrova EM, Marchenkou N (2018) Heat shock factor 1 confers resistance to lapatinib in ERBB2-positive breast cancer cells. *Cell Death and Disease*, 9: 621.
22. Eustace AJ, Conlon NT, McDermott MSJ, Browne BC, O'Leary P, Holmes FA, *et al* (2018) Development of acquired resistance to lapatinib may sensitise HER2-positive breast cancer cells to apoptosis induction by obatocicx and TRAIL. *BMC Cancer*, 18: 965.



ISSN: 0975-8542

Journal of Global Pharma Technology

[HOME](#) [ABOUT](#) [LOGIN](#) [REGISTER](#) [ARCHIVES](#) [SUBMISSIONS](#) [INSTRUCTIONS TO AUTHORS](#) [EDITORIAL TEAM](#) [DOWNLOAD](#) [CONTACTUS](#)

Home / Journal of Global Pharma Technology



[Current Issue](#)
[Past Issues](#)
[Articles in Press](#)

JGPT Dedicated In Honour Of Great Scientist



Robert Hooke (1635-1703)
father of Microscopy

Journal of Global Pharma Technology

It is our immense pleasure to launch **Journal of Global Pharma Technology (JGPT)** from December 2009, to cater to the publication needs of teachers, scientists, scholars and students. We thank all the forces with us, in the form of eminent advisory board and editorial board for all their cooperation and enthusiastic involvement in this blooming endeavor.

Journal publishes peer-reviewed original research papers, case reports, systematic reviews. The journal allows free access to its contents, which is likely to attract more readers and citations to articles published in JGPT.

JGPT publishes original research work that contributes significantly to the scientific knowledge in pharmacy and pharmaceutical sciences- Pharmaceutics, Novel Drug Delivery, Pharmaceutical Technology, Cosmeticology, Biopharmaceutics and Pharmacokinetics, Pharmacognosy, Natural Product Research, Medicinal Chemistry, Computational Chemistry and Molecular Drug Design, Pharmaceutical Analysis, Pharmacology, Pharmacy Practice, Clinical and Hospital Pharmacy, Cell Biology, Genomics and Proteomics, Pharmacogenomics, Bioinformatics, Biotechnology and Applied Computer Technology.

For this purpose we would like to ask you to contribute your excellent papers in pharmaceutical sciences. Currently, there are several papers under review consideration for the upcoming issues. I certainly hope that more ground will be covered in the future issues.

I hope you find this journal informative and useful. It is a new initiative. Your comments will help us improve the quality and content of the journal.



User

Username

Password

Remember me

[Login](#)

Journal Content

Search

Search Scope

All

[Search](#)

Browse

[» By Issue](#)

[» By Author](#)

[» By Title](#)



Editorial Team



Prof. (Dr.) Chakka Gopinath

Professor and Principal

Annamacharys College of Pharmacy

Thallapaka Panchayath, New Boyanapalli, Rajampet, Kadapa, A.P., India

Prof. (Dr.) A. Pandurangan

Dean/ Principal

Global School of Pharmacy, Global University, Saharanpur, U.P., India

Dr. Varaprasad Bobberala

Chief Scientist,

Translational Research Institute of Molecular Sciences (TRIMS)

Dr. Bhaskar C. Behera

Scientist,

Agharkar Research Institute (Dept. of Science & Technology, Govt. Of India), Plant Science Division, Pune, India

Dr. Nisha Tanwar

Dept. of Computer Science, Faculty of Science

Bhupal Nobles University, Udaipur, Rajasthan (India)

Prof. (Dr.) Ayad F. Alkaim

Professor

Department of Chemistry, Babylon University, Iraq

Table of Contents

Articles

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| The Comparative Analysis of Asthma Treatment in Pediatric Patients of Russia and China | PDF |
| Yue Li | |
| Liver Regenerative and Hepatoprotective Effects OF Moringa Oleifera Extract in the Liver Fibrosis Animal Model | PDF |
| Supriono Supriono | |
| Clinical Assessment of the use of Sublimated Mare's Milk in Complex Therapy of Mild and Moderate Psoriasis | PDF |
| Bakytgul Yermekbayeva | |
| Increasing of Early High-Risk Pregnancy Detection with Proactive Intervention in Bangkalan District, Madura Indonesi | PDF |
| Budi Prasetyo | |
| The Study of Structural- Mechanical and Physicochemical Properties of the Drug Antimicrobial and Anesthetic Action | PDF |
| Viktoriya Tarasenko | |
| Potential Protective Effect of Atriplex halimus Extract toward the Doxorubicin - Induced Apoptotic Gene Expression, Genetic and Hepatic Toxicity in Mice | PDF |
| Shenouda M. Girgis | |
| Identification of Microrna in Pediatric Latent Tuberculosis: A Preliminary Study in Indonesia | PDF |
| Ayling Sanjaya | |
| Correlation Family Support on Independence of Patients Schizophrenic Activities Daily Living (ADL) | PDF |
| Ronal Surya Aditya | |
| Effects of DHA-Enriched Fish Oil Supplements on Dopamine Receptor Gene Expression in the Cerebral Cortex and Hippocampus Related to the Male Rat's Weight Gain | PDF |
| Fifi Veronica | |

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| <p>Theater Performing Art: a Strategy to Improve Self-efficacy and Social Support in Patient with Type 2 diabetes Mellitus (T2DM)</p> <p>Mahendro Prasetyo Kusumo</p> | PDF |
| <p>The Characteristic of Congenital Fetal Anomalies at Sanglah Birth Defect Integrated Center (SIDIC), Sanglah General Hospital, Bali Indonesia</p> <p>Giri Chandra</p> | PDF |
| <p>Temporary Loop Occlusion using Vessel Loops on Bilateral Common iliac Arteries to Reduce Blood Loss in Total Abdominal Hysterectomy on Adherent Placenta Patient at Sanglah General Hospital, Bali-Indonesia</p> <p>I Nyoman Semadi</p> | PDF |
| <p>Long Term Use of Ovarian Stimulation Drugs May Affect Thyroid Function</p> <p>Ajile Elttayef</p> | PDF |
| <p>Nanoparticles Suspensions as Optical Power Limiting Synthesis and Characterization</p> <p>Gofran Hadi</p> | PDF |
| <p>Assessment of Pregnancy Complications among Internally Displaced Women in Karbala Governorate</p> <p>Ridha M. Iefta</p> | PDF |
| <p>Salmonella enterica Serovar Enteritidis and Typhimurium: Phenotypic, Molecular Detection and Sequencing of Quorum Sensing</p> <p>Zainab Adil Ghani Chabuck</p> | PDF |
| <p>Correlation of Serum Cu and Zn with Some Cytokines in Major Depressive Disorder</p> <p>Husein Kadhem Al-Hakeim</p> | PDF |
| <p>Evaluation of the Efficiency of the Isolated Fungi from Some Insect Species on White Fly Larvae: Bemisia Tabaci (Hemiptera: Aleyrodidae)</p> <p>H.D. Abdal-Jabar</p> | PDF |
| <p>Molecular Detection of Extended Spectrum-Beta Lactamase Producing Escherichia coli Isolated from Pregnant Women Infected with Urinary Tract Infection</p> <p>Oday Mitib Hadi</p> | PDF |

Different Molecular Methods to Determine Genetic Diversity in *Pseudomonas aeruginosa* Clinical Isolates

PDF

Reem Akram Najji

Plasma Diagnostics of Low Pressure Helium Glow Discharges at Different Working Voltages

PDF

Hanaa E. Jasim

Taxonomic Study of the Genus *Phlomis* L. (Lamiaceae) in Iraq Based on Trichome and Palynological Characters

PDF

Shaemaa Muhi Hasson

Effect the Magnetic Water on Physiological Traits of Callus the Fenugreek (*Trigonella foenum graecum* L.)

PDF

Basheer Abdulhamza Alalwani

The Effects of Stress on the Levels of Some Biochemical Parameters in Patients Intended to Surgery

PDF

Hayder Abbas Alwan

Changes of Phytochemical, Antioxidant Characteristics of Sunflower Seed Roasting

PDF

Minh Phuoc Nguyen

Physico-Chemical Attributes of Soursop Fruits during Storage under Treatment of 1-Methylcyclopropene (1-MCP)

PDF

Minh Phuoc Nguyen

Chemical Quality Attributes of Refrigerated Mudskipper (*Pseudapocryptes elongatus*) under Vacuum and Modified Atmosphere Packaging

PDF

Minh Phuoc Nguyen

Modified Atmosphere Packaging on Physico-Chemical Characteristics of Star Apple (*Chrysophyllum cainito*) Fruit during Post-harvest Storage

PDF

Minh Phuoc Nguyen

Investigate the Role of *Weissella Confuse* on TNF- α in Serum and Liver Tissue of Mice Infected with *Leishmania Donovanii*

PDF

Dhilal Abdulelah Ibraheem

Study the Effect of the Seed Grape *vitis vinifera* Plant Extract on Some Pathogenic Bacteria and Fungi

PDF

Sumayah Sami Hashim

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <p>The Potential Healing Properties of Systemic Probiotic-Prebiotic Supplement on Angular Cheilitis</p> <p>Malath Nabil Jafar</p> | <p>PDF</p> |
| <p>Study UV-Visible and FTIR Characterization of ZnPc Dye using Double Solvent</p> <p>Ban Mazin Alshabander</p> | <p>PDF</p> |
| <p>Evaluation the Antibacterial Effect of Rosemary and Lemon Grass Essential Oils against Planktonic and Biofilm of MRSA</p> <p>Zainab Zamel Khalaf</p> | <p>PDF</p> |
| <p>Thermal Resistance of Epoxy Resin and Phenol Formaldehyde Compound Mixed with Mixed Inhibitors</p> <p>Mustafa A. Rajab</p> | <p>PDF</p> |
| <p>In Vitro Evaluation and Post-thawing Activation of Najdi, Arabi (Najdi × arabi) Rams Spermatozoa Using Amino Acids and Pentoixfilline Added to Tris Extender</p> <p>Bushra F. Hassan</p> | <p>PDF</p> |
| <p>Application of Surgical Safety Checklist (WHO) at Al- Diwaneyah Teaching Hospital</p> <p>Ali Jawad Hamza Al-Shammari</p> | <p>PDF</p> |
| <p>Simple, Selective and Sensitive Spectrophotometric Method for Determination of Trace Amounts of Lead (II), Cademum (II), Cobalt (II) with Organomercury Compounds</p> <p>Fatima K. Aziz</p> | <p>PDF</p> |
| <p>Synthesis of Some New Pyrazoline Compounds Derived from α-β Unsaturated Compounds and Study their biological and Biochemical Effect</p> <p>Wissam M. R. Al-Joboury</p> | <p>PDF</p> |
| <p>Case History of Severe Toxicallergic Dermatitis in Patient with Acute Leukemia</p> <p>Igor Y. Gadaev</p> | <p>PDF</p> |
| <p>Pharmacological Study of Schiff Base Derived from Amoxicillin Drug and Vanillin</p> <p>Huda K. Khassaf</p> | <p>PDF</p> |
| <p>Association of Heat Shock Proteins (HSP70), Reactive Oxygen Species and Inflammatory Mediators in Male Infertility</p> <p>Nuha Yaarub Al-Harbi</p> | <p>PDF</p> |

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| <p>Effect of Topical Serratiopeptidase on Facial Wound Healing in Rabbit</p> <p>Faehaa A. Al-Mashhadanee</p> | PDF |
| <p>Synthesis and Characterization of Some Oxazepine Compounds from 2-Amino Thiazole</p> <p>Zainab Muhsin Bdaiwi</p> | PDF |
| <p>Corrosion Protection Enhancement using Electropolymerized Aniline Coating on Carbon Steel Pipelines in Industrial Water</p> <p>Abdulkareem M.A. Al-Sammarrai</p> | PDF |
| <p>Asymptomatic Tremendous Lung Shadow in a Young Man: A Case Report</p> <p>Li Min Wang</p> | PDF |
| <p>Psychogenic Depression Depending on Gender and Age Differentiation</p> <p>Alena Gura</p> | PDF |
| <p>Determination of Potential Compounds of Stevia Leaves (Stevia rebaudiana Bertoni) Against DPP4 as Candidates for Antidiabetic Drugs</p> <p>Resmi Mustarichie</p> | PDF |
| <p>Evaluation of Aggressive Behaviour Management in PICU (Psychiatric Intensive Care Unit): A Focus Group Study</p> <p>Ah. Yusuf</p> | PDF |
| <p>Integrated View of Formaldehyde in Lung Toxicity: Molecular Mechanisms, Cellular Aberrations and Pathological Considerations</p> <p>Soheir E. Kotob</p> | PDF |
| <p>An Update of In Vitro Fertilization-Intra Cytoplasmic Sperm Injection: A Review of Sperm Selection Methods</p> <p>Marianne Ingrid Aror</p> | PDF |
| <p>Wharton's Jelly Derived Mesenchymal Stem Cells: A Comparison Study in Preterm vs. Term Deliveries and in FBS vs. PRP vs Mesencult Culture Media</p> <p>Gita Pratama</p> | PDF |
| <p>Male Infertility: An Epidemiological and Clinical Profile at the Andrology Unit of Dr. Soetomo Hospital, Surabaya, Indonesia</p> <p>Antonius Wahyudi</p> | PDF |

| | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|
| <p>Complications of TVT Treatment of Stress Urinary Incontinence in Women</p> <p>Georgi Hubchev</p> | <p>PDF</p> |
| <p>Erythrocyte Changes in Death after General Over Cooling</p> <p>Revo Z. Alekseev</p> | <p>PDF</p> |
| <p>Study of Anti-Herpetic Activity of a Soft Dosage form With Acyclovir and Miramistin</p> <p>Kienko LS</p> | <p>PDF</p> |
| <p>Analysis of the study sample of patients and their use of antihypertensive drugs in monotherapy</p> <p>Tetiana Nehoda</p> | <p>PDF</p> |
| <p>Risk Factors Recurrent Respiratory Papilloma (RRP) on Juvenile and Adult Type in Tertiary Hospital, Indonesia</p> <p>Rizka Fathoni Perdana</p> | <p>PDF</p> |
| <p>Risk Behavior of Tiom Community Related with Helminthiasis at Lanny Jaya District, Papua Province, Indonesia</p> <p>Gurendro Putro</p> | <p>PDF</p> |
| <p>Electronic Cigarettes Use Characteristics Among Smokers in Indonesia</p> <p>Susi Ari Kristina</p> | <p>PDF</p> |
| <p>Evaluation of Nucleated Red Blood Cell Morphology Flag Screening with ADVIA® 2120</p> <p>R. Mustarichie</p> | <p>PDF</p> |
| <p>Semiautomated On-line for the Determination of Sitagliptin Phosphate using UV-low Pressure Mercury Lamp at 184.9 nm and 253.7 nm at ISNAG-fluorimeter Analyzer</p> <p>Nagam S. Turkey Al-Awadie</p> | <p>PDF</p> |
| <p>The Efficacy of Hydraulic Pressure Sinus Lift VS osteotome Lift via Crestal Approach Utilizing Sinus Endoscopy (Randomized Clinical Study)</p> <p>Aseel Hamid Madab</p> | <p>PDF</p> |
| <p>Effect Specific Cooling Times on Motility and Membrane Integrity of Cauda Epididymal Bovine Bull Sperm</p> <p>Asmaa Sh. Aliawy</p> | <p>PDF</p> |

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------|
| <p>Evaluation the Efficiency of Magnesium Oxide Nanoparticles in the Reduction of Ochratoxin A and in the Inhibition of Asperillusniger</p> <p>Shahbaa H Majeed</p> | PDF |
| <p>Characterization of the Dielectric Barrier Discharge (DBD) Plasma Jet for Staphylococcus Aureus Bacteria Deactivation</p> <p>Mohammed K. Khalaf</p> | PDF |
| <p>In Silico Study of Anti-Inflammatory Potential of 1,8-Cineole against Cox-2 and TLR-2</p> <p>Sianiwati Goenharo</p> | PDF |
| <p>Neuropathy in Vitamin Deficiency</p> <p>Shahdevi NK</p> | PDF |
| <p>The Effect of Nimodipine towards Calcium Ion (Ca²⁺) Expression in SH-SY5Y Neuron Cell Culture Exposed By Chronic Hyperglycaemia</p> <p>Shahdevi NK</p> | PDF |
| <p>The Effect of Ethanol on the Fetal Heart Muscle</p> <p>Galina Zhanaidarova</p> | PDF |
| <p>Systemic Corticosteroids are Effective in about a Half of pemphigus Patients</p> <p>Anfisa Lepekhova</p> | PDF |
| <p>The Study of Morbidity Structure in Children Using Automated Computer Technology</p> <p>Dmitriy Karlov</p> | PDF |
| <p>Mastication Profile and Alternative Healthy Mastication Model using Coconut Frond Shaving in Karo Women</p> <p>Ulina Karo-Karo</p> | PDF |
| <p>The Effect of Intracanal Medicament Using Calcium Hydroxide in Root Canal Infection Toward MMP-9, TIMP-1 and EGF Level in Apical Lesion: a Literature Review</p> <p>Ni Kadek Eka Widiadnyani</p> | PDF |
| <p>Physical Stability of Commonly Used Medication Administered by Parenteral Nutrition Admixtures in Hospital: A Systematic Review</p> <p>Erza Genatrika</p> | PDF |
| <p>A survey of quality of life among elderly population in Yogyakarta: A questionnaire-based study</p> <p>Dani Hanif Koncoro, Susi Ari Kristina</p> | PDF |

Breast cancer awareness and breast screening practice among women in Yogyakarta

[PDF](#)

Susi Ari Kristina, Nada Nisrina Salsabila

Awareness of Chronic Kidney Disease among General Adult Population in Indonesia

[PDF](#)

Susi Ari Kristina, Laksmi Anggun Larasati, Suci Hanifah

Antioxidant Activity, Formulation, and Evaluation of Roselle Seed Oil Extract Nanoemulsions

[PDF](#)

Arpa Petchsomrit

Development of Extemporaneously Prepared Captopril Oral Dosage Forms - A Comprehensive Chronological Study

[PDF](#)

Ayman M. Al-Qaaneh

Effect of Topical Laportea Decumana Leaves Extract on Labor Pain and Cortisol Level in the First Active Phase of Inpartu Condition

[PDF](#)

Sisma HL

Comparative Characteristics of QT Interval Measurements on ECG Performed Manually and by Automated Method in Male Patients at Rest

[PDF](#)

Vadim A. Dulskiy

Treatment of Childhood and Adolescent Depression with Physical Rehabilitation

[PDF](#)

Olga Taranina

Synthesis, Characterization and Biological Study of the Ligand 2-methyl-5-[(2E)-2-(4-Nitrobenzylidene) Hydrazinyl]- 1, 3, 4-Oxadiazole with some of its Transition Metal Complexes

[PDF](#)

Zainab M. Kareem

Determination of Diethyl Amine by Stop Flow Technique

[PDF](#)

Dakhil Nassir Taha

Application of the Mamdani Fuzzy Logic Multi Output Method to Maintain Electrical Conductivity in Hydroponic Media for Lettuce (*Lactuca sativa L.*) and Bok Choy (*Brassica rapa L.*)

[PDF](#)

Nyi Mekar Saptarini, Mohamad Nurkamal Fauzan

The Effect of Extract Ciplukan (*Physalis angulata L.*) to Placental Vessels, Placental Weight and Fetal Birth Weight in Preeclampsia Rat Model

[PDF](#)

Nur Permatasari

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <p>Anredera Cordifolia Leaves Sub-fraction as Anti Hyperlipidemia</p> <p>R. Mustarichie</p> | <p>PDF</p> |
| <p>Cytological Diagnosis of Ovarian Tumors</p> <p>Ahmed Al Qteishat</p> | <p>PDF</p> |
| <p>Clinical Correlates of the Severity of Diabetic Foot Ulcers</p> <p>Rahadyan Magetsari, Meirizal Hasan, Yossie Atyandhari</p> | <p>PDF</p> |
| <p>A Capillary Electrophoretic Method for the Analysis of Bupivacaine and Its Metabolites</p> <p>Roza Askarova</p> | <p>PDF</p> |
| <p>Clopidogrel as an Oral Antiaggregant in Ischemic Heart Disease</p> <p>Truong Dinh Cam</p> | <p>PDF</p> |
| <p>The Development of Nursing Diagnosis Based on Indonesian Nursing Diagnosis Standard of Patient with Schizophrenia in Hospital</p> <p>Rizki Fitriyasaki</p> | <p>PDF</p> |
| <p>The Impact of Age and Parity in the Incident of Premature Rupture Membranes (PRM)</p> <p>Tinuk Esti Handayani</p> | <p>PDF</p> |
| <p>Human Sperm Chromatin Maturation: A Study of Prolactin Supplementation in Sperm Preparation</p> <p>Silvia W Lestari</p> | <p>PDF</p> |
| <p>Health Coaching to Improve Mother's Self Efficacy in the Implementation of Prevention Malnutrition in Children</p> <p>Yuni Sufyanti Arief</p> | <p>PDF</p> |
| <p>The Comparison of Macular Thickness in Diabetic Patients without Proliferative Diabetic Retinopathy using Optical Coherence Tomography (OCT) at Prof. Dr. R D Kandou General Hospital, Manado, Indonesia</p> <p>Ade John Nursalim</p> | <p>PDF</p> |
| <p>The Recurrence of Stricture in Postoperative Patients at Dr. Soetomo Hospital from 2013-2017: A Case-Control Study</p> <p>I Dewa Gede Reza Sanjaya</p> | <p>PDF</p> |
| <p>Endophytic Fungi from Piper retrofractum VAHL: Isolation, Phytochemical Analysis, Antibacterial and Antioxidant Activities</p> <p>Dwi Koko Pratoko</p> | <p>PDF</p> |

Molecular Docking of Benzoylurea Derivatives as Potential Anti-Breast Cancer Agent and Its Admet Profiles

PDF

Siswandono Siswandono

Food Poisoning and Its Prevention on the Example of Listeria Monocytogenes

PDF

Ekaterina Savelyeva

Donor Site Morbidity after Anterior Iliac Bone Graft Harvesting

PDF

Rahadyan Magetsari

Gallic Acid, a Promising Chemopreventive Agent, Antagonizes Breast Cancer: Molecular Mechanisms of Action from Cell Culture Studies

PDF

Hanaa H Ahmed

Results of the Comparative Analysis of the Willingness-To-Pay Threshold Indicators for Introduction of Innovative Technologies in Healthcare Calculated on the Basis of the Purchasing Power Parity of the Population in Ukraine, Azerbaijan, Armenia, and Georgia

PDF

Hanna Panfilova

Single Nuclear Polymorphisms of VEGF, TGF- β 1, MMP9 Genes in Type 2 Diabetic Foot Ulcer Patients in Indonesian Population: A Case Control Study

PDF

Dedy Pratama

Molecular Detection of New Delhi Metallo Beta Lactamase 1 (NDM-1) - Producing Salmonella Typhi in Patients with Typhoid Fever

PDF

Qasim S. Al-Mayah

Analysis of Factors Affecting the Participation of Women of Childbearing Age in Visual Inspection with Acetic Acid (VIA) in The Community Health Center of Bangkalan

PDF

Uswatun Khasanah, Siti Anisak, Nurlailis Saadah, Esyuananik Esyuananik, Anis Nurlaili