SINTESIS HIBRID ISOINDOLINON-4-AMINOKUINOLIN (3-BENZIL-2-(6-((7-KLOROKUINOLIN-4-IL)AMINO)HEKSIL)-3-HIDROKSIISOINDOLIN-1-ON) SEBAGAI ANTIPLASMODIUM

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INTISARI

Telah dilakukan penelitian sintesis hibrid isoindolinon-4-aminokuinolin (3-benzil-2-(6-((7-klorokuinolin-4-il)amino)heksil)-3-hidroksiisoindolin-1-on). Selain itu, juga dilakukan uji antiplasmodium secara *in vitro* terhadap senyawa hibrid.

Sintesis senyawa hibrid dilakukan dalam 3 tahap. Tahap pertama yaitu sintesis 3-benziliden-1-ftalid melalui reaksi Sonogashira terkatalisis CuI antara asam 2-iodobenzoat dan fenilasetilen. Tahap kedua yaitu sintesis *N*-(7-klorokuinolin-4-il)heksana-1,6-diamin melalui reaksi substitusi nukleofilik aromatik antara 4,7-diklorokuinolin dan heksametilendiamin. Pada tahap ketiga, kedua senyawa digabungkan melalui reaksi adisi nukleofilik menghasilkan hibrid 3-benzil-2-(6-((7-klorokuinolin-4-il)amino)heksil)-3-hidroksiisoindolin-1-on. Produk dikarakterisasi menggunakan spektrometer FTIR, ^{1}H-NMR, dan ^{13}C-NMR, serta diuji aktivitas antiplasmodium secara *in vitro* terhadap *Plasmodium falciparum* 3D7.

Reaksi adisi nukleofilik antara 3-benziliden-1-ftalid dan *N*-(7-klorokuinolin-4-il)heksana-1,6-diamin menghasilkan senyawa hibrid 3-benzil-2-(6-((7-klorokuinolin-4-il)amino)heksil)-3-hidroksi-isoindolin-1-on berupa pasta kuning dengan persen hasil sebesar 60%. Nilai IC_{50} dari senyawa hibrid adalah 0,02 µM dan tergolong sebagai senyawa yang sangat aktif terhadap plasmodium sehingga berpotensi dikembangkan sebagai antimalaria.

Kata kunci: senyawa hibrid, isoindolinon, 4-aminokuinolin, antiplasmodium, 3-benziliden-1-ftalid

SYNTHESIS OF ISOINDOLINONE-4-AMINOQUINOLINE HYBRID OF 3-BENZYL-2-(6-((7-CHLOROQUINOLINE-4-YL)AMINO)HEXYL)-3-HIDROXYISOINDOLIN-1-ONE AS AN ANTIPLASMODIAL AGENT

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ABSTRACT

Synthesis and evaluation of isoindolinone-4-aminoquinoline hybrid of 3-benzyl-2-(6-((7-chloroquinoline-4-yl)amino)hexyl)-3-hydroxyisoindolin-1-one have been carried out. In addition, the object of this study was to perform the *in vitro* antiplasmodial assay.

Synthesis of hybrid was conducted in three steps. Initially, 3-benzyledene-1-phtalide was synthesized *via* Sonogashira coupling between 2-iodobenzoic acid and phenylacetylene in the presence of Cu(I) catalyst. Then, *N*-(7-chloroquinoline-4-yl)hexane-1,6-diamine was prepared *via* aromatic nucleophilic substitution reaction between 4,7-dichloroquinoline and hexametylenediamine. Both of products were combined *via* nucleophilic addition to give hybrid of 3-benzyl-2-(6-((7-chloroquinoline-4-yl)amino)hexyl)-3-hydroxyisoindolin-1-one. Finally, the products were characterized using FTIR, ^{1}H-NMR, and ^{13}C-NMR spectrometers, and the hybrid was subjected to *in vitro* against *Plasmodium falciparum* 3D7.

Nucleophilic addition reaction of 3-benzylidene-1-phtalide and *N*-(7-chloroquinoline-4-yl)hexane-1,6-diamine generated hybrid of 3-benzyl-2-(6-((7-chloroquinoline-4-yl)amino)hexyl)-3-hydroxyisoindolin-1-one in 60% yield as yellow paste. The IC_{50} of the hybrid is 0.02 µM and classified as very active compound against *Plasmodium falciparum.* Therefore, it has a great potential to be developed as an antimalarial.

Keywords: hybrid compound, isoindolinone, 4-aminoquinoline, antiplasmodial, 3-benzylidene-1-phtalide