

INTISARI

Parasetamol merupakan senyawa derivat *p*-aminofenol yang memiliki efek analgesik-antipiretik. Meskipun parasetamol memiliki efikasi dan keamanan yang baik, parasetamol tidak terlepas dari efek samping hepatotoksik. Hepatotoksisitas ini terjadi karena penggunaan parasetamol pada dosis besar secara akut maupun kronis. Modifikasi struktur *p*-aminofenol dapat dilakukan untuk menemukan senyawa derivat *p*-aminofenol yang diduga memiliki aktivitas analgesik lebih poten dan kurang hepatotoksik dibandingkan parasetamol. Penelitian ini bertujuan untuk mensintesis dan melakukan uji aktivitas analgesik dari derivat *p*-aminofenol, yaitu 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol.

Senyawa 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol disintesis dengan mereaksikan *p*-aminofenol dan vanillin dalam suasana asam. Hasil sintesis diuji kemurniannya dengan penetapan titik lebur dan Kromatografi Lapis Tipis. Kristal murni dielusidasi strukturnya dengan spektroskopi IR, ¹H-NMR, ¹³C-NMR, dan LC-MS. Aktivitas analgesik dari 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol diuji secara *in vivo* dengan metode geliat (*writhing test*). Sebanyak 30 ekor mencit jantan galur Balb/C dibagi menjadi 5 kelompok. Kelompok I sebagai kontrol negatif (CMC-Na 0,5%), kelompok II sebagai kontrol positif (parasetamol dosis 100 mg/kgBB), dan kelompok III-V sebagai kelompok perlakuan (senyawa hasil sintesis dengan varian dosis 81 mg/kgBB; 162,5 mg/kgBB; dan 324,5 mg/kgBB). Data kumulatif jumlah geliat dan respon analgesik dianalisis secara statistik menggunakan uji *one-way* ANOVA (taraf kepercayaan 95%). Jika hasilnya berbeda signifikan maka analisis statistik dilanjutkan dengan *Post Hoc Test Tukey*.

Berdasarkan hasil interpretasi data spektroskopi, diperoleh fakta bahwa senyawa 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol berhasil disintesis. Senyawa 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol hasil sintesis berbentuk serbuk kuning dengan titik lebur sebesar 225,1-234,6 °C dan rendemen sintesis sebesar 76,21%. Berdasarkan hasil uji aktivitas analgesik dengan metode *writhing test*, senyawa sintesis dosis 81 mg/kgBB; 162,5 mg/kgBB; dan 324,5 mg/kgBB berturut-turut memiliki persentase daya analgesik sebesar 44,13 ± 26,72 %; 37,14 ± 19,82 %; dan 44,92 ± 14,97 %. Senyawa 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol terbukti memiliki aktivitas analgesik, dan pada dosis 81 mg/kgBB memiliki aktivitas analgesik yang tidak berbeda signifikan dengan parasetamol dosis 100 mg/kgBB.

Kata kunci: 4-[N-(4'-hidroksifenil)karboksimidoil]-2-metoksifenol, *p*-aminofenol, parasetamol, analgesik, *writhing test*

ABSTRACT

Paracetamol is an analgesic-antipyretic compound derived from *p*-aminophenol. Though paracetamol has good efficacy and safety on consumption, paracetamol has hepatotoxicity as its adverse effects. The hepatotoxicity of paracetamol is caused by acute or chronic consumption of high-dose paracetamol. Structure modification of *p*-aminophenol can be done to find another *p*-aminophenol derivative compounds that have analgesic effect more potent and less hepatotoxic than paracetamol. One of this *p*-aminophenol derivative is 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound. The purpose of this research is to synthesize 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound and to evaluate its analgesic activity.

4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound was synthesized through reaction of *p*-aminophenol and vanillin under acid condition. The purity of the synthesized products were determined using melting point determination and Thin Layer Chromatography. The structure of obtained pure crystals were elucidated using IR spectroscopy, ¹H-NMR spectroscopy, ¹³C-NMR spectroscopy, and LC-MS. The analgesic evaluation of 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound was carried in vivo using writhing test method. As much as 30 Balb/c strain mice were divided into 5 groups. Group I acted as negative control (CMC-Na 0,5%), group II acted as positive control (paracetamol 100 mg/kg), and group III to V acted as the test group (the synthesized products with three varied dosages: 81 mg/kg; 162,5 mg/kg; and 324,5 mg/kg). The total writhes and analgesic responses from each group were statistically analyzed using one-way ANOVA (level of confidence 95%). If the results said to be significantly different, the statistic analysis were continued using Post Hoc Test Tukey.

From the spectroscopy data interpretation, it was known that 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound was successfully synthesized. The 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound has an appearance of yellow powder, with the melting point of 225,1-234,6 °C, and product rendement of 76,21%. From the analgesic activity evaluation using writhing test methods, the test compound of the dose 81 mg/kg; 162,5 mg/kg; and 324,5 mg/kg each has analgesic potency of 44,13 ± 26,72 %; 37,14 ± 19,82 %; and 44,92 ± 14,97 %. It was proved that 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol compound has analgesic activity, and on dose 81 mg/kg the compound has analgesic activity that not differ than paracetamol 100 mg/kg.

Keywords: 4-[N-(4'-hydroxyphenyl)carboxyimidoil]-2-methoxyphenol, *p*-aminophenol, paracetamol, analgesic, writhing test