

SINTESIS TURUNAN HIDROKSIBENZOFENON DAN UJI AKTIVITASNYA SEBAGAI TABIR SURYA SERAPAN LEBAR SERTA ANTIOKSIDAN

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INTISARI

Sintesis 2,4,4'-trihidroksi-3'-metoksibenzofenon (**6**); 2,3,4,4'-tetrahidroksi-3'-metoksibenzofenon (**7**); 2,4,4'-trihidroksi-3-metil-3'-metoksibenzofenon (**8a**); 3,4',5-trihidroksi-4-metil-3'-metoksibenzofenon (**8b**) dan 3-heksil-2,4',6-trihidroksi-3'-metoksibenzofenon (**9**) telah dilakukan. Uji sitotoksitas, aktivitas tabir surya, fotostabilitas, dan antioksidan senyawa **6-9** telah berhasil ditentukan.

Sintesis turunan hidroksibenzofenon, yaitu **6-9** masing-masing dilakukan melalui reaksi asilasi antara asam vanilat (**1**) dengan turunan fenol berupa resorsinol (**2**), pirogalol (**3**), 2-metilresorsinol (**4**), atau 4-*n*-heksilresorsinol (**5**) dengan bantuan katalis $\text{CH}_3\text{SO}_3\text{H}$ dan agen dehidrasi P_4O_{10} (reagen Eaton). Masing-masing produk sintesis dimurnikan dengan kromatografi kolom menggunakan gradien eluen *n*-heksana : etil asetat (dari non polar ke polar) dilanjutkan analisis dengan scanner KLT. Produk hasil pemurnian dianalisis menggunakan spektrometer FTIR, *direct inlet* MS (DI-MS), ^1H - dan ^{13}C -NMR. Uji sitotoksitas **6-9** dengan 3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazolium bromida (MTT) dilakukan pada sel Vero. Senyawa **6-9** diformulasikan menjadi krim tabir surya (**N6-9**) dan diukur nilai *Sun Protection Factor* (SPF), panjang gelombang kritis (λ_{kritis}), peringkat perlindungan UVA, serta fotostabilitas. Senyawa **6-9** diuji aktivitas antioksidan dengan 2,2-difenil-1-pikrilhidrazil (**DPPH**).

Eksperimen sintesis menghasilkan senyawa yang diinginkan dengan persen hasil untuk **6**, **7**, **8**, dan **9** adalah masing-masing 61, 28, 10, dan 11%. Uji sitotoksitas **6-9** menghasilkan nilai IC_{50} masing-masing 605, 699, 457, dan 279 $\mu\text{g mL}^{-1}$. Krim yang telah dibuat dari **6-9** (**N6-9**) memiliki nilai SPF masing-masing 47, 70, 36, dan 17 dan tergolong tabir surya serapan lebar pada masing-masing λ_{kritis} 386, 386, 387, dan 387 nm dengan perlindungan UVA paling baik (peringkat perlindungan UVA = 4). Krim tabir surya (**N6-9**) menghasilkan sifat fotostabil sampai menit ke-90 yang diindikasikan dengan nilai SPF > 10. Senyawa **6-9** menunjukkan aktivitas antioksidan dengan nilai EC_{50} masing-masing sebesar $2,60 \times 10^2$; $3,36 \times 10^0$; $3,49 \times 10^2$; dan $3,86 \times 10^2 \text{ mg L}^{-1}$ daripada kontrol positif antioksidan, butil hidroksi toluen (**BHT**), yang memiliki EC_{50} sebesar $1,40 \times 10^1 \text{ mg L}^{-1}$.

Kata kunci: antioksidan, fotostabilitas, hidroksibenzofenon, reagen Eaton, sitotoksitas

SYNTHESIS OF HYDROXYBENZOPHENONE DERIVATIVES AND THEIR ACTIVITY TESTING AS BROAD SPECTRUM SUNSCREEN AND ANTIOXIDANT

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ABSTRACT

Synthesis of 2,4,4'-trihydroxy-3'-methoxybenzophenone (**6**); 2,3,4',4-tetrahydroxy-3'-methoxybenzophenone (**7**); 2,4,4'-trihydroxy-3'-methoxy-3-methylbenzophenone (**8a**); 3,4',5'-trihydroxy-3'-methoxy-4-methylbenzophenone (**8b**) and 3-hexyl-2,4',6'-trihydroxy-3'-methoxybenzophenone (**9**) have been carried out. Cytotoxicity, sunscreen activity, photostability, and antioxidant assays of **6-9** have been determined.

Synthesis of hydroxybenzophenones, i.e. **6-9** have been conducted through acylation reaction between vanillic acid (**1**) and phenol derivatives, such as resorcinol (**2**), pyrogallol (**3**), 2-methylresorcinol (**4**), or 4-*n*-hexylresorcinol (**5**) with CH₃SO₃H catalyst and P₄O₁₀ as dehydration agent (Eaton's reagent), respectively. Each of synthesized products was purified using column chromatography with eluent gradient *n*-hexane : ethyl acetate (from non polar to polar) and the products were then analyzed using TLC scanner. The purified products were analyzed using FTIR, direct inlet MS (DI-MS), ¹H- and ¹³C-NMR spectrometer. Cytotoxicity assay of **6-9** using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were done in Vero cell line. Compounds **6-9** were formulated as sunscreen creams (**N6-9**) and were measured their Sun Protection Factor (SPF) values, critical wavelength ($\lambda_{critical}$), UVA protection rating, and photostability. Compounds **6-9** were tested antioxidant activity using 2,2-diphenyl-1-picrylhydrazyl (DPPH).

The synthesis experiments afforded the expected products in the percent yield for **6-9** were 61, 28, 10, dan 11%, respectively. The results of the **6-9** cytotoxicity assay produced IC₅₀ values of 605, 699, 457, and 279 $\mu\text{g mL}^{-1}$, respectively. Sunscreen creams made from **6-9** (**N6-9**) have SPF values of 47, 70, 36, and 17 respectively and are classified as broad spectrum sunscreens at $\lambda_{critical}$ 386, 386, 387, and 387 nm respectively with UVA protection is best (UVA protection rating = 4). The creams (**N6-9**) produced photostable properties up to 90 minutes that is indicated with SPF values > 10. Compounds **6-9** show antioxidant activity with an EC₅₀ value of 2.60×10^2 ; 3.36×10^0 ; 3.49×10^2 ; and $3.86 \times 10^2 \text{ mg L}^{-1}$ respectively compared to positive antioxidant control, butylated hydroxytoluene (BHT), having an EC₅₀ of $1.40 \times 10^1 \text{ mg L}^{-1}$.

Keywords: antioxidant, cytotoxicity, Eaton's reagent, hydroxybenzophenone, photostability