

**SINTESIS SENYAWA SERI
ALKOKSIFENILKALIKS[4]RESORSINARENA SEBAGAI
ANTIOKSIDAN DAN ANTIKANKER, SERTA ESTER ALKOKSIFENIL-
KALIKS[4]RESORSINARIL OKTABENZOAT/OKTASINAMAT
SEBAGAI TABIR SURYA**

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INTISARI

Penelitian ini bertujuan untuk mensintesis senyawa kaliks[4]resorsinarena yang berpotensi dikembangkan sebagai antioksidan, antikanker dan tabir surya. Sintesis senyawa alkoksifenilkaliks[4]resorsinaril oktabenzoat/oktasinamat, yaitu C-4-aliloksi-fenilkaliks[4]-resorsinaril oktabenzoat (AFKB); C-4-aliloksi-3-metoksifenilkaliks[4]-resorsinaril oktabenzoat (AMFKB); C-4-etoksifenilkaliks[4]resorsinaril oktabenzoat (EFKB); C-4-aliloksi-fenilkaliks[4]resorsinaril oktasinamat (AFKS); C-4-aliloksi-3-metoksifenilkaliks[4]resorsinaril oktasinamat (AMFKS) dan C-4-etoksifenilkaliks[4]-resorsinaril oktasinamat (EFKS), dilakukan melalui reaksi esterifikasi C-4-aliloksi-fenilkaliks[4]resorsinarena (AFK), C-4-aliloksi-3-metoksifenilkaliks[4]resorsinarena (AMFK) dan C-4-etoksifenilkaliks[4]resorsinarena (EFK) dengan benzoil klorida atau sinamoil klorida dengan katalis piridina. Sintesis senyawa AFK, AMFK dan EFK dilakukan melalui reaksi kondensasi resorsinol berturut-turut dengan 4-aliloksibenzaldehida, 4-aliloksi-3-metoksibenzaldehida dan 4-etoksi-benzaldehida menggunakan katalis asam klorida dalam pelarut etanol. Senyawa 4-aliloksibenzaldehida dan 4-aliloksi-3-metoksibenzaldehida disintesis melalui reaksi alilasi 4-hidroksibenzaldehida dan 4-hidroksi-3-metoksibenzaldehida (vanilin) menggunakan alilbromida dengan katalis logam natrium dalam pelarut etanol; senyawa 4-etoksibenzaldehida disintesis melalui reaksi etilasi 4-hidroksibenzaldehida menggunakan dietilsulfat dalam larutan natrium hidroksida.

Uji aktivitas antioksidan terhadap senyawa AFK, AMFK, EFK menggunakan metode DPPH (2,2-difenil-1-pikrilhidrazil) menunjukkan aktivitas antioksidan EFK paling tinggi dengan nilai $IC_{50} = 72,72 \mu\text{g/mL}$ (kuersetin $IC_{50} = 29,59 \mu\text{g/mL}$). Uji aktivitas antikanker terhadap senyawa AFK, AMFK dan EFK menggunakan metode MTT (3-(4,5-dimetiltiazol-2-il)-2,5-difeniltetrazolium bromida) menunjukkan senyawa AMFK dan EFK masing-masing memiliki aktivitas sitotoksik yang lemah terhadap sel HeLa dan T47D. Berdasarkan perhitungan Indeks Selektivitas (IS), senyawa HFK (senyawa pembanding) memiliki nilai IS paling tinggi dibandingkan dengan AFK, AMFK dan EFK.

Uji tabir surya terhadap senyawa AFKB, AMFKB, EFKB, AFKS, AMFKS dan EFKS menunjukkan keenam senyawa menyerap radiasi UV pada daerah UVB dan UVC. Nilai SPF paling tinggi dimiliki oleh AMFKS dan EFKS pada konsentrasi 40 $\mu\text{g/mL}$ yaitu 148,57 dan 139,50. Hasil uji fotostabilitas keenam senyawa ester relatif baik. Uji sitotoksitas menunjukkan keenam senyawa bersifat tidak toksik terhadap sel Vero. Uji proteksi dilakukan terhadap AMFKS dan EFKS (nilai SPF tertinggi dan fotostabilitas cukup baik) masing-masing didapatkan nilai IC_{50} sebesar 27,53 $\mu\text{g/g}$ dan 28,46 $\mu\text{g/g}$ (Pabanox[®] $IC_{50} = 0,00 \mu\text{g/g}$).

Kata kunci: sintesis, kaliks[4]resorsinarena, antioksidan, antikanker, tabir surya

SYNTHESIS OF ALKOXYPHENYLCALIX[4]RESORCINARENE SERIES COMPOUNDS AS ANTIOXIDANT AND ANTICANCER, AND ALKOXYPHENYLCALIX[4]RESORCINARIL OCTABENZOIC / OCTACINNAMIC ESTERS AS SUNSCREENS

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ABSTRACT

The aims of this study were to synthesize the calix[4]resorcinarene compounds that are potentially developed as antioxidants, anticancer, and sunscreen. The syntheses of alkoxyphenylcalix[4]resorsinaril octabenzoate/octacinnamate, i.e C-4-allyloxyphenylcalix[4]resorcinaril octabenzoate (AFKB); C-4-allyloxy-3-methoxyphenylcalix[4]resorcinaril octabenzoate (AMFKB); C-4-ethoxyphenylcalix[4]resorcinaril octabenzoate (EFKB); C-4-allyloxyphenylcalix[4]resorcinaril octacinnamate (AFKS); C-4-allyloxy-3-methoxyphenylcalix[4]resorcinaril octacinnamate (AMFKS), and C-4-ethoxyphenylcalix[4]resorcinaril octacinnamate (EFKS) were conducted by esterification of C-4-allyloxyphenylcalix[4]resorcinarene (AFK), C-4-allyloxy-3-methoxyphenylcalix[4]resorcinarene (AMFK), and C-4-ethoxyphenylcalix[4]resorcinarene (EFK) by using a benzoyl chloride or a cinnamoyl chloride with pyridine as a catalyst. The syntheses of AFK, AMFK, and EFK were carried out by condensation reaction of resorcinol with 4-allyloxybenzaldehyde, 4-allyloxy-3-methoxybenzaldehyde, and 4-ethoxybenzaldehyde, respectively, in ethanol with hydrochloric acid as a catalyst. The 4-allyloxybenzaldehyde and 4-allyloxy-3-methoxybenzaldehyde were synthesized by the reaction of the 4-hydroxybenzaldehyde and 4-hydroxy-3-methoxybenzaldehyde (vanillin) via allylation reaction using an allylbromide with the sodium metal as a catalyst in ethanol. The 4-ethoxybenzaldehyde was synthesized by the ethylation of 4-hydroxybenzaldehyde using diethyl sulfate in the sodium hydroxide solution.

The antioxidant activity assays were performed on AFK, AMFK, EFK compounds which was evaluated by DPPH (2,2-diphenyl-1-picrylhydrazil) method showed EFK has the highest antioxidant activity with $IC_{50} = 72.72 \mu\text{g/mL}$ (quercetine $IC_{50} = 29.59 \mu\text{g/mL}$). Anticancer evaluation were performed on AFK, AMFK, EFK compounds by MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide) method showed that AMFK and EFK compound each has a weak cytotoxic activity against HeLa and T47D cells. Based on calculations, the selectivity Index (SI) value of EFK compound (comparative compound) is the highest compared to AFK, AMFK and EFK.

The sunscreen test towards AFKB, AMFKB, EFKB, AFKS, AMFKS, and EFKS revealed that the compounds absorb UV radiation in UVB and UVC regions. AMFKS and EFKS showed the highest SPF values at concentrations of 40 $\mu\text{g/mL}$ by 148.57 and 139.50, respectively. The photostability test showed that stability of all compounds was relatively good for all esters. The cytotoxicity test showed that all compounds is not toxic to the Vero cells. The protection test was performed on AMFKS and EFKS (the best SPF and good photostability) showed IC_{50} values of 27,53 $\mu\text{g/g}$ and 28.46 $\mu\text{g/g}$, respectively, (Pabanox[®] $IC_{50} = 0.00 \mu\text{g/g}$).

Keywords: synthesis, calix[4]resorcinarene, antioxidant, anticancer, sunscreens