SYNTHESIS AND PRELIMINARY EVALUATION OF SEVERAL CHALCONE DERIVATIVES AS SUNSCREEN COMPOUNDS

Jumina Jumina [a*], Rizky Woro Styaningrum [a], Dwi Siswanta [a], Sugeng Triono [a],
Yoga Priastomo [a], Harizal Harizal [b], Eti Nurwening Sholikhah [c], Abdul Karim Zulkarnain [d]

[a]Department of Chemistry, Faculty of Mathematics and Natural Science, Gadjah Mada University,
Sekip Utara Bulaksumur, Sleman, Yogyakarta 55281, Indonesia
[b]Department of Public Health, Faculty of Health Sciences, Esa Unggul University, Jakarta 11510, Indonesia
[c]Department of Pharmacology and Therapy, Faculty of Medicine, Gadjah Mada University,
Sekip Utara Bulaksumur, Sleman, Yogyakarta 55281, Indonesia
[d]Department of Pharmaceutics, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta 55291, Indonesia
[*]e-mail: jumina@ugm.ac.id

Abstract. Four chalcone derivatives containing chloro and methoxy substituents were synthesized and pre-evaluated as broad-spectrum UV protector with intrinsic antioxidant activity. UV absorbance of chalcones **1-4** showed a wide range of UV absorbance values in UVB and UVA regions (λ_{max}= 310-360 nm) and molar absorptivity values (ε= 14,000-20,000 M^{-1}cm^{-1}). Chalcones **3** and **4** showed better photostability than chalcones **1** and **2** because the lowering of their absorbance was smaller and slower under UVB irradiation. A combination of the spectra of chalcone derivatives **1-4** indicated that a formulation containing all four will provide a broad-spectrum sunscreen protecting the skin from UVA and UVB.

Introduction

It is well known that exposure to UV radiation induces the formation of reactive oxygen species that further cause oxidative stress in the epidermis and dermis layers of skin. The presence of oxidative stress leads to various negative effects on skin such as erythema or inflammation [1], skin cancer [2,3], and photoaging [4]. To protect from these undesirable effects, the skin needs a double protection system that protects the skin not only from outside by using sunscreen compound that acts as protective shield from UV radiation but also from inside utilizing antioxidant that quenches the reactive oxygen species formed [5-7]. Commonly, both of these functions are generated by two different active compounds by adding an antioxidant such as ascorbic acid or tocopherol/tocotrienol into the sunscreen formulation [8]. However, the use of two or more active compounds with different physicochemical properties in one formulation complicates the formulation process since there are several factors that need be considered such as compatibility, stability, penetrability, and amount of added antioxidant [6]. Therefore, further development and optimization is required in order

to obtain the active compounds that have ideal sunscreen characteristics (broad-spectrum, higher molar absorptivity and photostability, and lower toxicity) and antioxidant activity (higher antioxidant capacity and stability, and lower toxicity).

Chalcones are a group of compounds that have high antioxidant activity, particularly for the skin [9-12]. They can be easily synthesized and functionalized to form derivatives that have a broad range of λ_{max} (280-365 nm) and relatively high molar absorptivity (ε= 20,000-30,000 M^{-1}cm^{-1}) [13-15]. Besides that, chalcones also have relatively low toxicity to human dermal fibroblast cells [16], and various positive effects related to skin health such as antipigmentation [17-23], anticarcinogenic [24] and antitumor [25]. Therefore, they are quite safe to be applied on the skin surface. These benefits highlight that chalcones have great potency and can be developed as broad-spectrum sunscreen with intrinsic antioxidant properties. Furthermore, modification of the chalcones by incorporating electron withdrawing and donating groups can be implemented easily to shift the λ_{max} to UVA, UVB, or UVC regions. It is hypothesized that

combining the chalcones with different λ_{max} in a formulation would definitely produce a broad-spectrum sunscreen.

This paper describes the synthesis of (E)-chalcone, (E)-4'-chlorochalcone, (E)-4-methoxychalcone and (E)-3,4-dimethoxychalcone, as well as investigation of their potency as sunscreen compound through measurement of their UV spectra either as a single compound or a mixture of chalcones, calculation of their sun protection factor (SPF) values, and their photostability study under the influence of UVB radiation. The results obtained in this study would show the potency of chalcones as sunscreen compounds.

Experimental
Generalities

All materials were purchased from Merck (Darmstadt, Germany) and used directly without any purification unless otherwise indicated.

Reaction monitoring and purity test were conducted through thin-layer chromatography (TLC) analysis on aluminum sheets silica gel 60 F_{254} plates (Merck) with UV lamp (Sigma-Aldrich) at 254 nm as detecting unit (eluent: *n*-hexane/ethyl acetate in 3:2 ratio).

Melting point values were measured on an Electrothermal 9100 and are uncorrected.

IR spectra were recorded on a FTIR Shimadzu Prestige-21. GC-MS analyses were performed using a GC-MS Shimadzu QP-2010S.

NMR spectra were obtained on a JEOL JNM-ECA500 [1]H 500 MHz and [13]C 125 MHz.

UV spectra were measured with Milton Roy Spectronic 3000 Array spectrophotometer and chloroform was used as the solvent. Before measuring the UV absorbance of samples, a background correction was performed using quartz cuvettes of 1 cm path length (L) filled with blank solvent. Photostability tests were conducted using UVB lamp with energy distribution of 0.2678 mW/cm^2.

General procedure for the synthesis of chalcones

Acetophenone (3.65 mmol) in ethanol (3 mL) was added to aqueous KOH (6.5 mL 13% w/v) solution and the mixture was stirred until homogenous. The mixture was added dropwise to benzaldehyde (3.65 mmol) in ethanol (3 mL) and stirred for 20 hours at room temperature. The reaction mixture was poured into ice-water and acidified using 10% HCl (v/v) solution until pH 3. The precipitate formed was collected through vacuum filtration and recrystallized from ethanol. The product was dried and characterized.

(E)-chalcone 1. The reaction was conducted using the general procedure described above by using acetophenone (0.44 g, 3.65 mmol), benzaldehyde (0.39 g, 3.65 mmol), and KOH (0.85 g, 15 mmol) affording a pale yellow solid (0.57 g, 75%), m.p. 52-53°C; IR (KBr pellet, cm^{-1}): 1658 (C=O), 972 (C=C trans); UV (CHCl$_3$) λ_{max}= 310 nm; ^{1}H-NMR (CDCl$_3$) δ 8.03 (*d*, 2H, *J*= 14.9 Hz); 7.80 (*d*, 1H, *J*= 15.6 Hz); 7.63 (*dd*, 1H, *J*= 14.9 Hz and 15.6 Hz); 7.57 (*t*, 1H, *J*= 7.5 Hz and 10 Hz); 7.52 (*d*, 1H, *J*= 14.9 Hz); 7.49 (*d*, 2H, *J*= 15.6 Hz); 7.41 (*t*, 2H, *J*= 5 Hz and 7.5 Hz); ^{13}C-NMR (CDCl$_3$) δ: 190.89 (C=O), 145.11 (C=C trans), 138.10 (C$_{Ar}$), 134.81 (C$_{Ar}$), 133.02 (C$_{Ar}$), 130.72 (C$_{Ar}$), 129.03 (C$_{Ar}$), 128.73 (C$_{Ar}$), 128.60 (C$_{Ar}$), 128.57 (C$_{Ar}$), 122.00 (C=C trans); MS: m/z calcd. 208.26; found 208.00 (M$^+$).

(E)-4'-chlorochalcone 2. The reaction was conducted using the procedure described previously by using 4-chloroacetophenone (0.56 g, 3.65 mmol), benzaldehyde (0.39 g, 3.65 mmol), and KOH (0.85 g, 15 mmol) affording a pale yellow solid (0.54 g, 61%), m.p. 91-93°C; IR (KBr pellet, cm^{-1}): 1658 (C=O), 979 (C=C trans), 763 (C-Cl); UV (CHCl$_3$) λ_{max}= 313 nm; ^{1}H-NMR (CDCl$_3$) δ 7.96 (*d*, 2H, *J*= 15.6 Hz); 7.80 (*d*, 1H, *J*= 16.3 Hz); 7.64 (*dd*, 1H, *J*= 15.6 Hz and 16.3 Hz); 7.47 (*t*, 3H, *J*= 7.50 Hz and 7.50 Hz); 7.42 (*t*, 3H, *J*= 2.50 Hz and 5.00 Hz); ^{13}C-NMR (CDCl$_3$) δ: 189.20 (C=O), 145.43 (C=C trans), 139.30 (C-Cl), 138.55 (C$_{Ar}$), 134.76 (C$_{Ar}$), 130.87 (C$_{Ar}$), 130.03 (C$_{Ar}$), 129.11 (C$_{Ar}$), 129.03 (C$_{Ar}$), 128.64 (C$_{Ar}$), 121.51 (C=C trans); MS: m/z calcd. 242.70; found 242.00 (M$^+$).

(E)-4-methoxychalcone 3. The reaction was conducted using the procedure described previously by using acetophenone (0.44 g, 3.65 mmol), 4-methoxybenzaldehyde (0.50 g, 3.65 mmol), and KOH (0.85 g, 15 mmol) affording a pale yellow solid (0.53 g, 61%), m.p. 69-70°C; IR (KBr pellet, cm^{-1}): 1658 (C=O), 1265 (C-O-C), 979 (C=C trans); UV (CHCl$_3$) λ_{max}= 340 nm; ^{1}H-NMR (CDCl$_3$) δ 8.00 (*d*, 2H, *J*= 15.60 Hz); 7.77 (*d*, 1H, *J*= 14.1 Hz); 7.60 (*d*, 2H, *J*= 14.1 Hz); 7.56 (*t*, 1H, *J*= 7.75 Hz and 7.25 Hz); 7.48 (*t*, 2H); 7.40 (*d*, 1H, *J*= 15.6 Hz); 6.93 (*d*, 1H, *J* = 14.1 Hz); 3.86 (*s*, 3H); ^{13}C-NMR (CDCl$_3$) δ: 190.65 (C=O), 161.79 (-O-C$_{Ar}$), 144.82 (C=C trans), 138.57 (C$_{Ar}$), 132.70 (C$_{Ar}$), 130.37 (C$_{Ar}$), 128.68 (C$_{Ar}$), 128.52 (C$_{Ar}$), 119.80 (C=C trans), 114.53 (C$_{Ar}$), 55.40 (OCH$_3$) MS: m/z calcd. 238.29; found 238.00 (M$^+$).

(E)-3,4-dimethoxychalcone 4. The reaction was conducted using the procedure described previously by using acetophenone (0.44 g,

3.65 mmol), 3,4-dimethoxybenzaldehyde (0.61 g, 3.65 mmol), and KOH (0.85 g, 15 mmol) affording a bright yellow solid (0.86 g, 88%), m.p. 81-82°C; IR (KBr pellet, cm^{-1}): 1651 (C=O), 1265 (C-O-C), 979 (C=C trans); UV (CHCl$_3$) λ_{max}= 354 nm; ^{1}H-NMR (CDCl$_3$) δ 8.01 (*d*, 1H, *J*= 15.6 Hz); 7.77 (*d*, 1H, *J*= 14.9 Hz); 7.59 (*t*, 2H, *J*= 7.75 Hz and 7.25 Hz); 7.52 (*t*, 2H); 7.40 (*d*, 1H, *J*= 14.9 Hz); 7.24 (*d*, 1H, *J*= 15.6 Hz); 7.16 (*d*, 1H, *J*= 2.5 Hz); 6.91 (*d*, 1H); 3.95 (*s*, 3H); 3.93 (*d*, 3H); ^{13}C-NMR (CDCl$_3$) δ 190.69 (C=O), 151.44 (-O-C$_{Ar}$), 149.24 (-O-C$_{Ar}$), 145.06 (C=C trans), 138.48 (C$_{Ar}$), 132.59 (C$_{Ar}$), 128.58 (C$_{Ar}$), 128.15 (C$_{Ar}$), 127.86 (C$_{Ar}$), 123.22 (C$_{Ar}$), 120.07 (C=C trans), 111.09 (C$_{Ar}$), 110.01 (C$_{Ar}$), 56.09 (OCH$_3$), 56.02 (OCH$_3$); MS: m/z calcd. 268.31; found 268.00 (M$^+$).

Determination of the absorbance profile

The UV spectroscopy measurements was performed using a UV-Vis spectrophotometer to obtain the absorbance profile, λ_{max}, ε, and SPF values for each synthesized chalcone derivative. Before measuring the absorbance of each compound, optimization of concentration was conducted by preparing three solutions of different concentrations *i.e.* 50, 40, and 25 mg/L. The absorbance values of these three solutions were scanned in the range of 200-400 nm using 1cm quartz cuvettes against CHCl$_3$ as the blank solution. The concentration that produced a smooth line curve was selected for further measurement and calculation of λ_{max}, ε, and SPF values. Eqs. (1,2) were used to calculate ε and Sun Protection Factor (SPF) values, respectively [26]. Calculation of SPF value was conducted by utilizing the absorbance (A) of compounds in chloroform without preparing any formulation.

$$A = C \times \varepsilon \times c \qquad (1)$$

where, ε - molar absorptivity, M^{-1}cm^{-1};

　　L - path length of UV cm^{-1};

c - molar concentration, M.

$$A = -\log\left(\frac{1}{SPF}\right) = \log SPF \qquad (2)$$

Photostability test

Photostability tests were conducted based on the procedure developed by Chawla, H.M. *et al.* [27] with several modifications. A solution of the chalcone in CHCl$_3$ with optimized concentration was placed in a sealed quartz cuvettes of 1 cm path length and irradiated with UVB (energy distribution of 0.2678 mW/cm^2) for 0, 5, 15, 30, 60, and 90 minutes, respectively. The absorbance of solution was then recorded for each irradiation time in the 200-400 nm wavelength range. The results were analysed by comparing the lowering of absorbance at each irradiation time.

Results and discussion
Characterization of chalcones derivatives

Synthesis of chalcone derivatives as outlined in Scheme 1 was performed through Claisen-Schmidt condensation reaction by mixing an equimolar quantity of benzaldehyde and acetophenone derivatives in ethanolic KOH for 20 hours at room temperature. The chalcones were produced in moderate to good yield, and characterization of the reaction products were conducted using IR, GC-MS, ^{1}H and ^{13}C-NMR data.

The chalcones showed the presence of a conjugated double bond and carbonyl group (enone group) between two phenyl rings. The IR spectra of the products showed the lowering of absorbance from 1691-1692 cm^{-1} in acetophenone and 4-chloroacetophenone [28] to 1651 cm^{-1} in chalcone **4** and 1658 cm^{-1} in chalcones **1-3** indicating extension of the carbonyl group by the formed enone groups.
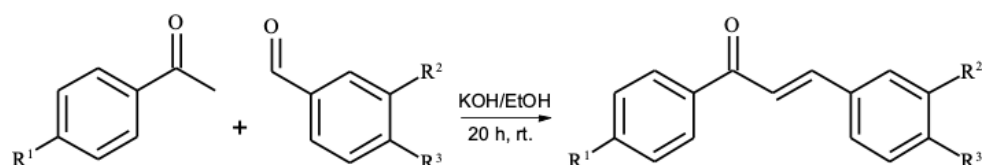
Chalcone	R^1	R^2	R^3
1	H	H	H
2	Cl	H	H
3	H	H	OCH$_3$
4	H	OCH$_3$	OCH$_3$

Scheme 1. Synthesis of chalcones 1-4.

The ^{1}H-NMR spectra also consistently showed that the coupling constants of *trans* protons were 14.9 Hz and 15.6 Hz in chalcone **1**, 15.6 Hz and 16.3 Hz in chalcone **2**, 15.6 Hz and 14.1 Hz in chalcone **3**, and 14.9 Hz and 15.6 Hz in chalcone **4**, respectively. These values indicated that the reaction products were formed in *trans* conformation of enone groups. In the sunscreen application, the *trans*-chalcones are preferred since they have λ_{max} in UVA and UVB regions, higher molar absorptivity, and better stability as compared to *cis*-chalcones [29]. In addition, the mass spectral data of chalcones **1-4** showed the presence of molecular ions at m/z of 208, 242, 238, and 268, respectively, further confirming the structures of the products.

Determination of the absorbance profile

Preliminary UV absorption evaluations were conducted using the optimized concentrations of 25 mg/L (1.20×10^{-4} M, 1.03×10^{-4} M, 1.05×10^{-4} M, and 9.33×10^{-5} M) for chalcones **1-4**, respectively. Determination of the absorbance profile (λ_{max}, ε, and SPF values) was conducted in the 200-400 nm wavelength range which represents three different regions of UV radiation *i.e* UVC (200-280 nm), UVB (280-320 nm), and UVA (320-400 nm). Absorbance measurements showed that chalcone derivatives **1-4** containing chloro and methoxyl groups have a wide range of λ_{max} in UVB-UVA regions (300-360 nm) and moderate molar absorptivity (14,000-20,000 $M^{-1}cm^{-1}$) (Figure 1 and Table 1).

The wide variation of UV absorbance indicated that these chalcone derivatives can be combined together in a broad-spectrum sunscreen formulation for skin protection against UVB and UVA radiations as shown in Figure 2. Furthermore, the usage of several active compounds from the same compound class will simplify formulation process since they would usually have the same physicochemical properties.
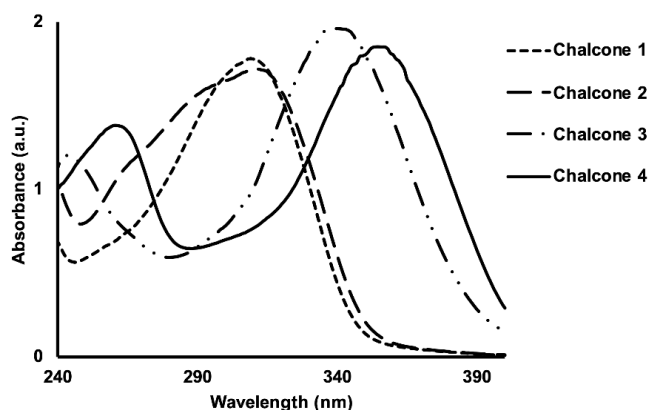
Theoretically, addition of certain functional groups in the A and B rings will affect λ_{max} of each chalcone derivative by shifting HOMO and LUMO energy levels modulating the $\pi \rightarrow \pi^*$ electron transition in absorption of UV radiation [30]. Thus, addition of electron donating and withdrawing groups will cause bathochromic and hypsochromic shifts, respectively. It is known that addition of a substituent in the B ring has a more significant effect on the UV absorption than in A ring [30,31]. This phenomenon can be observed in the UV absorbances of the studied chalcones. In chalcone **2**, the presence of a chloro group (a withdrawing group) at the C4 position in ring A caused a small bathochromic shift with a λ_{max} of 313 nm, while in chalcones **3** and **4**, presence of the methoxy groups (a strong electron donating group) caused relatively significant bathochromic shift with λ_{max} of 340 and 354 nm, respectively.

Chalcones **1-4** showed lower molar absorptivity compared to the values reported in the literature [13,15]. This was probably caused by solvation of the chalcones in different solvent used in the measurement (chloroform instead of ethanol). Generally, the usage of different solvent will affect λ_{max}, molar absorptivity (ε), bandwidth, and band shape of absorbance spectra. In this case, polar and non-polar solvents will increase molar absorptivity, while semi-polar solvents will decrease it [32].

Table 1

UV absorbance profile of chalcones 1-4.

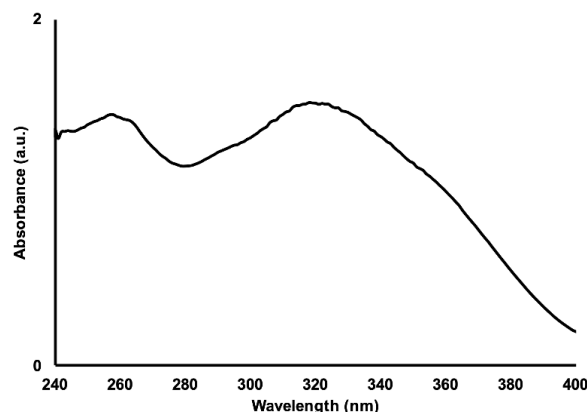| Chalcone	1	2	3	4
λ_{max} (nm)	310	313	340	354
UV region	UVB	UVB	UVA	UVA
A (a.u.)	1.784	1.713	1.960	1.848
ε ($M^{-1} cm^{-1}$)	14,867	16,631	18,667	19,807
SPF	60.81	51.64	91.20	70.47

Figure 1. UV Spectra of chalcone derivatives.

Figure 2. UV spectrum of the chalcones 1-4 mixture.

The calculated SPF values for each chalcone in the given concentration (25 mg/L) which were in the range of 51.6-91.2 in the UVB and UVA regions was a good indication for the potency of the synthesized chalcones as sunscreen compounds.

Photostability test

The photostability test was performed by observing and comparing the UV absorbance profile of the chalcone derivatives before and after UV irradiation (energy distribution of 0.2678 mW/cm^2) at different times (0, 5, 15, 30, 60, and 90 minutes). Figure 3(a),(b) and Figure 4(a),(b) show the UV spectra of four chalcone derivatives as a function of irradiation time. It is clear that the irradiation of chalcones **1** and **2** showed a quick lowering of absorbance at 310 and 313 nm, respectively, and a smaller increment at approximately 250-260 nm in the first 5 minutes (Figure 3 (a),(b)). These results indicate that chalcones **1** and **2** have a relatively low stability as compared to the other two chalcone derivatives that experience relatively smaller and slower changes in their UV spectra for even at 90 minutes. Several publications have reported that the interaction between the chalcone derivatives and UV radiation in solution possibly causes photoisomerization as indicated by the increment in absorption at 250-260 nm [13,29,33], and photodimerization to form cyclobutane derivatives [34,35].

There are at least two theories that can be used to explain higher photostability of chalcones **3** and **4** (Figure 4(a),(b)) compared to chalcones **1** and **2** (Figure 3(a),(b)). Firstly, chalcones **3** and **4** contain at least a methoxy group (strong electron donating group) at position 4 that contributes to the conjugated enone group present in these two compounds. This extension of the conjugated system changes the bond order in double and single bond between the two phenyl rings that eventually restricts and prevents the rotation in the *cis-trans* photoisomerization process [29,33]. On the contrary, the conjugation system in chalcone **2** is not very effective at increasing rigidities of the bonds between the two phenyl rings due to the lower ability of chloro group to participate in conjugation. Secondly, photoisomerization and photodimerization of chalcones are highly depended on the wavelength of UV radiation in which UVB or UVA radiation will significantly affect the stability of chalcone derivatives that absorb at the same wavelength [35].
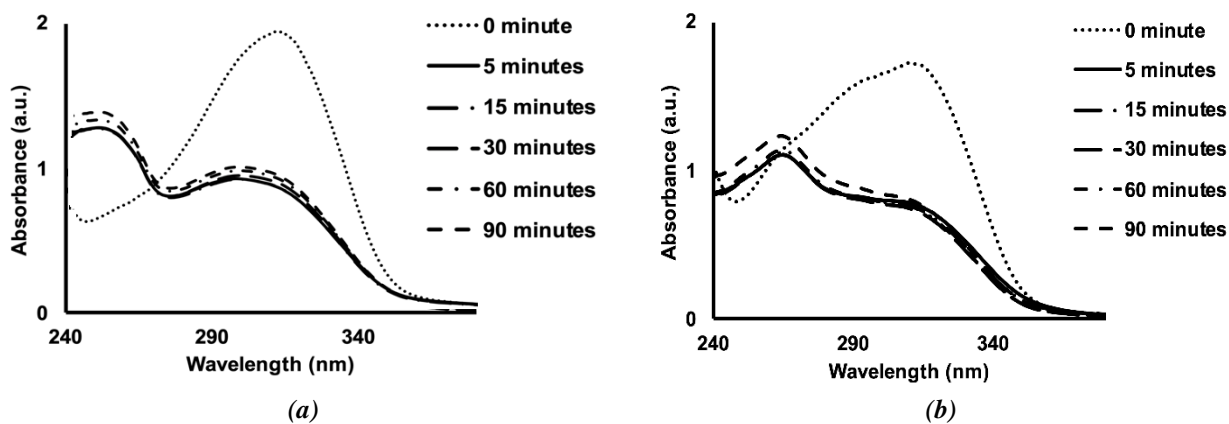

(a)   *(b)*

Figure 3. Photostability test of chalcone 1 *(a)* **and chalcone 2** *(b)***.**
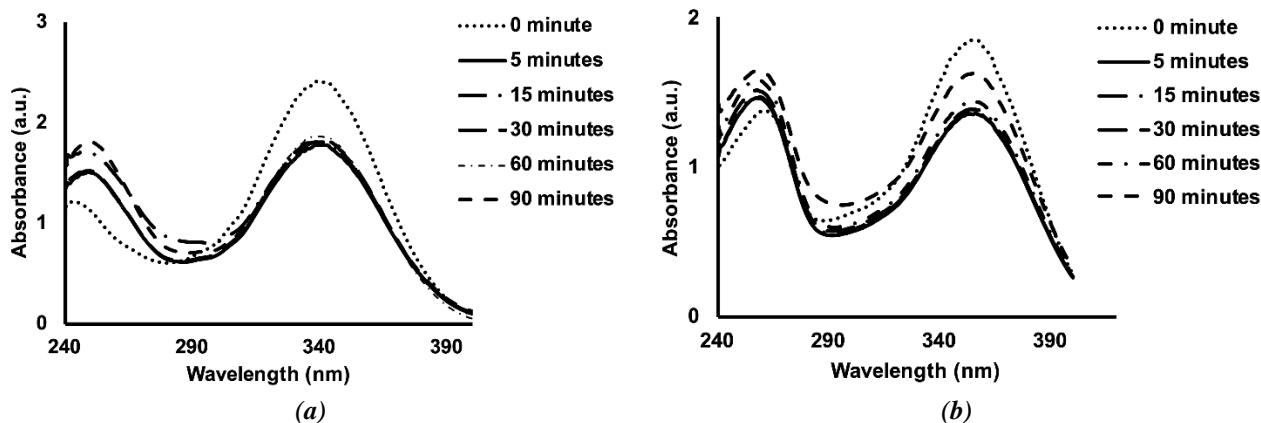

(a)   *(b)*

Figure 4. Photostability test of chalcone 3 *(a)* **and chalcone 4** *(b)***.**

UV radiation used in this experiment was in the range of UVB, therefore only chalcones **1** and **2** (absorb in the UVB region) were strongly affected by this irradiation as compared to chalcones **3** and **4** that absorb in the UVA region. However, to confirm the validity of these arguments, more experiments need to be conducted.

Conclusions

Four chalcone derivatives that show a wide range of λ_{max} covering UVB and UVA with moderate molar absorptivity have been synthesized in 61-88% yield. Chalcones **1**, **2**, **3**, and **4** showed λ_{max} respectively at 310, 313, 340, and 354 nm and gave promising SPF values in the range of 51.6-91.2 in the concentration of 25 mg/L. Chalcones **3** and **4** containing a 4-methoxy group were found to be more photostable in which absorbance reduction was smaller and slower compared to chalcones **1** and **2**.

Present studies indicate that a combination of these four chalcones could be used in a sunscreen formulation with a broad-spectrum of UV absorbance to protect the skin from UVB and UVA radiations.

Acknowledgments

References

1. Parrish, J.A.; Jaenicke, K.F.; Anderson, R.R. Erythema and melanogenesis action spectra of normal human skin. photochemistry and photobiology, 1982, 36(2), pp 187-191. DOI: https://doi.org/10.1111/j.1751-1097.1982.tb04362.x
2. Dahle, J.; Kvam, E. Induction of delayed mutations and chromosomal instability in fibroblasts after UVA, UVB, and X-radiation. Cancer Research, 2003, 63(7), pp. 1464-1469. https://cancerres.aacrjournals.org/content/63/7/1464
3. Jiang, Y.; Rabbi, M.; Kim, M.; Ke, C.; Lee, W.; Clark, R.L.; Mieczkowski, P.A.; Marszalek, P.E. UVA generates pyrimidine dimers in DNA directly. Biophysical Journal, 2009, 96(3), pp. 1151-1158. DOI: https://doi.org/10.1016/j.bpj.2008.10.030
4. Fisher, G.J.; Kang, S.; Varani, J.; Bata-Csorgo, Z.; Wan, Y.; Datta, S.; Voorhees, J.J. Mechanisms of photoaging and cronological skin aging. Archives of Dermatology, 2002, 138(11), pp. 1462-1470. DOI: 10.1001/archderm.138.11.1462
5. Velasco, M.V.R.; Sarruf, F.D.; Salgado-Santos, I.M.N.; Haroutiounian-Filho, C.A.; Kaneko, T.M.; Baby, A.R. Broad spectrum bioactive sunscreens. International Journal of Pharmaceutics, 2008, 363(1-2), pp. 50-57. DOI: https://doi.org/10.1016/j.ijpharm.2008.06.031
6. Oresajo, C.; Pillai, S.; Manco, M.; Yatskayer, M.; McDaniel, D. Antioxidants and the skin: understanding formulation and efficacy. Dermatologic Therapy, 2012, 25(3), pp. 252-259. DOI: https://doi.org/10.1111/j.1529-8019.2012.01505.x
7. de Paula, L.R.; Parussulo, A.L.A.; Araki, K.; Toma, H.E. Evaluation of sun protection factor of cosmetic formulations by a simple visual *in vitro* method mimicking the *in vivo* method. Journal of Pharmaceutical Sciences, 2011, 101(2), pp. 726-732. DOI: https://doi.org/10.1002/jps.22797
8. Chen, L.; Hu, J.Y.; Wang, S.Q. The role of antioxidants in photoprotection: a critical review. Journal of the American Academy of Dermatology, 2012, 67(5), pp. 1013-1024. DOI: https://doi.org/10.1016/j.jaad.2012.02.009
9. Yamamoto, T.; Yoshimura, M.; Yamaguchi, F.; Kouchi, T.; Tsuji, R.; Saito, M.; Obata, A.; Kikuchi, M. Anti-allergic activity of naringenin chalcone from a tomato skin extract. Bioscience, Biotechnology and Biochemistry, 2004, 68(8), pp. 1706-1711. DOI: https://doi.org/10.1271/bbb.68.1706
10. Popoola, O.K.; Marnewick, J.L.; Rautenbach, F.; Ameer, F.; Iwuoha, E.I.; Hussein, A.A. Inhibition of oxidative stress and skin aging-related enzymes by prenylated chalcones and other flavonoids from *Helichrysum teretifolium*. Molecules, 2015, 20(4), pp. 7143-7155. DOI: 10.3390/molecules20047143
11. Martinez, R.M.; Pinho-Ribeiro, F.A.; Steffen, V.S.; Caviglione, C.V.; Vignoli, J.A.; Baracat, M.M.; Georgetti, S.R.; Verri, Jr. W.A.; Casagrande, R. Hesperidin methyl chalcone inhibits oxidative stress and inflammation in a mouse model of ultraviolet B irradiation-induced skin damage. Journal of Photochemistry and Photobiology B: Biology, 2015, 148, pp. 145-153. DOI: https://doi.org/10.1016/j.jphotobiol.2015.03.030
12. Martinez, R.M.; Pinho-Ribeiro, F.A.; Vale, D.L.; Steffen, V.S.; Vicentini, F.T.M.C.; Vignoli, J.A.; Baracat, M.M.; Georgetti, S.R.; Verri, Jr. W.A.; Casagrande R. Trans-chalcone added in topical formulation inhibits skin inflammation and oxidative stress in a model of ultraviolet B radiation skin damage in hairless mice. Journal of Photochemistry and Photobiology B: Biology, 2017, 171, pp. 139-146. DOI: https://doi.org/10.1016/j.jphotobiol.2017.05.002
13. Black, W.B.; Lutz, R.E. Ultraviolet absorption spectra of chalcones. Identification of chromophores. Journal of the American Chemical Society, 1955, 77(19), pp. 5134-5140. DOI: https://doi.org/10.1021/ja01624a055

14. Tsukerman, S.V.; Orlov, V.D.; Lavrushin, V.F. Ultraviolet absorption spectra of chalcone analogs containing a selenophene nucleus. Chemistry of Heterocyclic Compounds, 1969, 5(1), pp. 55-57. DOI: https://doi.org/10.1007/BF01031764

15. Tejima, T.; Nakamura, K.; Hattori, M.; Masuda, S.; Imokawa, G.; Takaishi, N. Novel chalcone derivatives and ultraviolet absorbers comprising the same. US patent, 1986, No. 4,584,190.

16. Maydt, D.; De Spirt, S.; Muschelknautz, Ch.; Stahl, W.; Muller, T.J.J. Chemical reactivity and biological activity of chalcones and other α,β-unsaturated carbonyl compounds. Xenobiotica, 2013, 43(8), pp. 711-718. DOI: https://doi.org/10.3109/00498254.2012.754112

17. Nerya, O.; Musa, R.; Khatib, S.; Tamir, S.; Vaya, J. Chalcones as potent tyrosinase inhibitors: the effect of hydroxyl positions and numbers. Phytochemistry, 2004, 65(10), pp. 1389-1395. https://doi.org/10.1016/j.phytochem.2004.04.016

18. Nerya, O.; Vaya, J.; Musa, R.; Izrael, S.; Ben-Arie, R.; Tamir, S. Glabrene and isoliquiritigenin as tyrosinase inhibitors from *Licorice* roots. Journal of Agricultural and Food Chemistry, 2003, 51(5), pp. 1201-1207. DOI: https://doi.org/10.1021/jf020935u

19. Khatib, S.; Nerya, O.; Musa, R.; Shmuel, M.; Tamira, S.; Vaya, J. Chalcones as potent tyrosinase inhibitors: the importance of a 2,4-substituted resorcinol moiety. Bioorganic and Medicinal Chemistry, 2005, 13(2), pp. 433-441. DOI: https://doi.org/10.1016/j.bmc.2004.10.010

20. Jun, N.; Hong, G.; Ju, K. Synthesis and evaluation of 2',4',6'-trihydroxychalcones as a new class of tyrosinase inhibitors. Bioorganic and Medicinal Chemistry, 2007, 15(6), pp. 2396-2402. DOI: https://doi.org/10.1016/j.bmc.2007.01.017

21. Zhang, X.; Hu, X.; Hou, A.; Wang, H. Inhibitory effect of 2,4,2',4'-tetrahydroxy-3-(3-methyl-2-butenyl)-chalcone on tyrosinase activity and melanin biosynthesis. Biological and Pharmaceutical Bulletin, 2009, 32(1), pp. 86-90. DOI: https://doi.org/10.1248/bpb.32.86

22. Seo, W.D.; Ryu, Y.B.; Curtis-Long, M.J.; Lee, C.W.; Ryu, H.W.; Jang, K.C.; Park, K.H. Evaluation of anti-pigmentary effect of synthetic sulfonylamino chalcone. European Journal of Medicinal Chemistry, 2010, 45(5), pp. 2010-2017. DOI: https://doi.org/10.1016/j.ejmech.2010.01.049

23. Takahashi, M.; Takara, K.; Toyozato, T.; Wada, K. A novel bioactive chalcone of *Morus ausralis* inhibits tyrosinase activity and melanin biosynthesis in B16 melanoma cells. Journal of Oleo Science, 2012, 61(10), pp. 585-592. DOI: https://doi.org/10.5650/jos.61.585

24. Yagura, T.; Motomiya, T.; Ito, M.; Honda, G.; Iida, A.; Kiuchi, F.; Tokuda, H.; Nishino, H. Anticarcinogenic compounds in the uzbek medicinal plant, *Helichrysum maracandicum*. Journal of Natural Medicines, 2008, 62, pp. 174-178. DOI: https://doi.org/10.1007/s11418-007-0223-y

25. Akihisa, T.; Tokuda, H.; Hasegawa, D.; Ukiya, M.; Kimura, Y.; Enjo, F.; Suzuki, T.; Nishino, H. Chalcones and other compounds from the exudates of *angelica keiskei* and their cancer chemopreventive effects. Journal of Natural Products, 2006, 69(1), pp. 38-42. DOI: https://doi.org/10.1021/np058080d

26. Walters, C.; Keeney, A.; Wigal, C.T.; Johnston, C.R.; Cornelius, R.D. The spectrophotometric analysis and modeling of sunscreens. Journal of Chemical Education, 1997, 74(1), pp. 99-101. DOI: https://doi.org/10.1021/ed074p99

27. Chawla, H.M.; Pant, N.; Kumar, S.; Mrig, S.; Srivastava, B.; Kumar, N.; Black, D.StC. Synthesis and evaluation of novel tetrapropoxycalix[4]arene enones and cinnamates for protection from ultraviolet radiation. Journal of Photochemistry and Photobiology B: Biology, 2011, 105(1), pp. 25-33. https://doi.org/10.1016/j.jphotobiol.2011.06.007

28. Jones, R.N.; Forbes, W.F.; Mueller, W.A. The infrared carbonyl stretching bands of ring substituted acetophenones. Canadian Journal of Chemistry, 1957, 35(5), pp. 504-514. DOI: https://doi.org/10.1139/v57-071

29. Xue, Y.; Mou, J.; Liu, Y.; Gong, X.; Yang, Y.; An, L. An *ab initio* simulation of the UV/Visible spectra of substituted chalcones. Central European Journal of Chemistry, 2010, 8(4), pp. 928-936. DOI: https://doi.org/10.2478/s11532-010-0058-3

30. Szmant, H.H.; Basso, A.J. The absorption spectra of substituted chalcones. Journal of the American Chemical Society, 1952, 74(17), pp. 4397-4400. DOI: https://doi.org/10.1021/ja01137a047

31. Shin, D.-M.; Song, D.-M.; Jung, K.-H.; Moon, J.-H. Photochemical transformation of chalcone derivatives. Journal of Photoscience, 2001, 8(1), pp. 9-12. https://pdfs.semanticscholar.org/a8d6/a4bdd1118239fac7f9888f829ace1a09d142.pdf

32. Agrapidis-Paloympis, L.E.; Nash, R.A.; Shaath, N.A. The effect of solvents on the ultraviolet absorbance of sunscreens. Journal of Cosmetic Sicence, 1987, 38(4), pp. 209-221. http://journal.scconline.org/abstracts/cc1987/cc038n04/p00209-p00221.html

33. Yayli, N.; Ucuncu, O.; Aydin, E.; Gok, Y.; Yasar, A.; Baltaci, C.; Yildirim, N.; Kucuk, M. Stereoselective photochemistry of heteroaryl chalcones in solution and the antioxidant activities. Journal of Photochemistry and Photobiology A: Chemistry, 2005, 169(3), pp. 229-234. DOI: https://doi.org/10.1016/j.jphotochem.2004.06.015

34. Yayli, N.; Ucuncu, O.; Yasar, A.; Gok, Y.; Kucuk, M.; Kolayli, S. Stereoselective photochemistry of methoxy chalcones in solution and their radical scavenging activity. Turkish Journal of Chemistry, 2004, 28(4), pp. 515-521. https://journals.tubitak.gov.tr/chem/issue.htm?id=545

35. Nicodem, D.E.; Matos, J.A. de M.G. Photoisomerization of chalcone: wavelength dependence. Journal of Photochemistry, 1981, 15(3), pp. 193-202. DOI: https://doi.org/10.1016/0047-2670(81)87003-7