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Physical and Chemical Stability of Formulations Loaded with Taxifolin Tetra-octanoate

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Chemically stable ester derivatives of taxifolin have become a focus of interest for their role in the satisfactory effects on human health. Accordingly, the aim of this study was to evaluate the physical and chemical stability of different formulations containing 0.02% taxifolin tetra-octanoate, which was proved to possess higher inhibitory effect on tyrosinase activity compared with taxifolin in a cell-free system. In the studies of physical stability, a Brookfield viscometer was used to determine rheological behavior of formulations containing taxifolin tetra-octanoate, and a portable pH meter was used to determine pH change. Moreover, chemical stability was determined by HPLC with UV detection. Formulations were evaluated for 12 weeks stored at 25 and 40°C. Results showed that storage time had no significant influence on viscosity of the formulations containing taxifolin tetra-octanoate, and pH value was relatively stable, which was within the limits of normal skin pH range. In the chemical stability studies, taxifolin tetra-octanoate in the essence formulation was most unstable at 40°C with about 81% degradation in 12 weeks of storage, however, the percentage of remaining taxifolin tetra-octanoate in cream formulation stored for 12 weeks at 25°C was the highest, about 93%. The results in this study may contribute to the development of more stable formulations containing taxifolin tetra-octanoate.

Key words stability; formulation; taxifolin tetra-octanoate; rheology; chromatography

Introduction

Flavonoids, a large group of phenolic compounds, constitute a class of abundant secondary metabolites in plants.^{1–3} Flavonoids have attracted more and more attention because of their rich pharmacological and antioxidant activities.^{4,5} The difference of the chemical structure of flavonoids influences their activities, expresses strong interrelation with the number and position of hydroxyl groups and the situation of glycosylation or alkylation.^{6,7}

Taxifolin (3,5,7,3',4'-pentahydroxy flavanone or dihydroquercetin) belongs to the category of flavonoids,⁸ which is mainly found in many kinds of plants,^{9–11} such as fruit (especially grapes, oranges and grapefruit),¹² vegetables, leaves, nuts, flowers and beverages (coffee, tea and wine).^{13–15} As flavonoid, taxifolin is mostly present in the form of glycosides and aglycones.

Because taxifolin possesses unique antioxidant activity and biological activity,^{16–18} it has plenty of positive effects on human health. Taxifolin plays a special role in eliminating excess free radicals,¹⁹ reducing the formation of cancer cells,²⁰

improving immune function,²¹ preventing and treating cardiovascular disease,²² and inhibiting the growth of *Streptococcus sobrinus*.²³ Furthermore, taxifolin is used in depigmentation drugs and whitening cosmetics due to its tyrosinase inhibitory capacity.^{24,25}

Although the effect of taxifolin is very extensive, taxifolin is poorly water soluble and has low stability, which greatly restricts its bioavailability and efficiency.²⁶ Therefore, for the purpose of enhancing the solubility and stability of taxifolin, it is necessary to synthesize taxifolin derivatives and further measure their characteristics. The objective of this study was to evaluate the stability of cosmetic formulations containing taxifolin tetra-octanoate (Fig. 1) which is an ester derivative of taxifolin that we synthesized previously.

Experimental

Materials Taxifolin (≥99.5%) was purchased from Zhengzhou FengYao Agricultural Science and Technology Co. (China). Mushroom tyrosinase and L-dihydroxyphenylalanine (L-DOPA) were obtained from Sigma-Aldrich Co. (St. Louis,

Fig. 1. Chemical Structures of Taxifolin and Taxifolin Tetra-octanoate

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MO, U.S.A.). Acetonitrile, methanol, ethanol and acetic acid were HPLC grade from Sigma. Other chemicals were of reagent grade and used without any further purification. Distilled water was used throughout the study.

Synthesis of Taxifolin Tetra-octanoate Taxifolin, 0.40 g (1.33 mmol), was dissolved in 15 mL anhydrous dioxane at room temperature. Octanoyl chloride, 1.12 mL (7.34 mmol), was added and the mixture was stirred for 10 min. Then, 0.58 mL (7.34 mmol) of anhydrous pyridine was added, and the mixture was continuously stirred for 4 h. Finally, the mixture was left to stand for 12 h at room temperature. The reactants were filtered and evaporated under reduced pressure. The residue was extracted with ethyl acetate (20 times volume) and the extract was washed with 3% NaHCO₃ solution and distilled water. Organic layers were dried over anhydrous MgSO₄ and evaporated under vacuum. TLC was performed on silica gel 60 F254 plates with *n*-hexane–dioxane (1:1, v/v) as the eluent (*R_f*, 0.91). Then, the crude product was purified by using silica gel column chromatography with *n*-hexane–dioxane (4:1, v/v) as the eluent. The resulting compound was a yellow powder, 0.99 g (86% yield), with approximately 95% purity of enantiomers.

¹H-NMR (500 MHz, CDCl₃) δ : 11.30 (1H, s), 7.36 (1H, dd, *J* = 10.5, 2.1 Hz), 7.30 (1H, d, *J* = 2.05 Hz), 7.26 (1H, m), 6.37 (1H, d, *J* = 2 Hz), 6.32 (1H, d, *J* = 2 Hz), 5.76 (1H, d, *J* = 12.05 Hz), 5.41 (1H, d, *J* = 12.05 Hz), 2.55 (4H, t, *J* = 7.5 Hz), 2.35 (4H, t, *J* = 7.5 Hz), 1.75 (2H, m), 1.65 (6H, m), 1.31 (32H, m), 0.89 (12H, m); ¹³C-NMR (125 MHz, CDCl₃) δ : 192.9, 179.9, 172.2, 171.2, 170.95, 170.93, 163.4, 161.6, 159.2, 143.2, 142.4, 133.5, 125.3, 124.0, 123.0, 80.6, 72.5, 34.5, 34.29, 34.25, 34.21, 33.8, 31.85, 31.82, 31.81, 31.7, 29.31, 29.30, 29.2, 29.1, 29.09, 29.06, 29.03, 25.1, 24.96, 24.92, 24.8, 22.8, 22.7, 14.2; electrospray ionization (ESI)-MS *m/z*: 831.4659 (Calcd for C₄₇H₆₈O₁₁Na [M + Na]⁺: 831.4762).

Tyrosinase Activity Assay The tyrosinase inhibitory activity of taxifolin tetra-octanoate was measured in a cell-free system. A premixture solution containing 0.175 M phosphate buffer (pH 6.8), 40 μ L of mushroom tyrosinase (1000 U/mL), and 20 μ L of test substance was incubated for 5 min at 37°C in a 96-well microplate. Then, 40 μ L of L-3,4-dihydroxyphenylalanine (L-DOPA) was added to the mixture solution in a total volume of 200 μ L. The assay mixture was incubated for 25 min at 37°C. After incubation, the optical density (OD) at 492 nm was measured to observe dopachrome formation. The tyrosinase activity was calculated as follows:

$$\text{Tyrosinase activity (\%)} = (C - D) / (A - B) \times 100$$

where A is OD with tyrosinase but without test substance; B is OD without test substance and tyrosinase; C is OD with test substance and tyrosinase; and D is OD with test substance but without tyrosinase.

Preparation of Formulations Compositions of the cream formulations are shown in Table 1. Firstly, the creams were prepared by heating part A at 80°C in a digital water bath, until the oil phase was dissolved completely. Then parts A and C were added to part B. Homogenization of the different phases was achieved with a homo-mixer (HY-001 A, Hansung-ENG, Korea) at stirring speed of 3000 rpm for 3 min and then reduced to 1500 rpm for 3 min, and finally the creams were cooled to room temperature while maintaining a stirring speed of 500 rpm for further 3 min, and finally degassed.

Table 1. Components of the Cream Formulations under Study

Components	Percentage of components in each formulation (w/w)	
	F1	F2
Part A		
Dimethicone/PEG-10/15 crosspolymer	15.00	15.00
Cyclopentasiloxane	5.00	5.00
Part B		
Distilled water	63.92	63.92
Glycerin	10.00	10.00
Glycosyl trehalose/Hydrogenated starch hydrolysate	1.00	1.00
Butylene glycol	5.00	5.00
Betaine	0.01	0.01
Disodium EDTA	0.05	0.05
Part C		
Taxifolin tetra-octanoate	0.02	
Taxifolin		0.02

Table 2. Components of the Lotion Formulations under Study

Components	Percentage of components in each formulation (w/w)	
	F3	F4
Part A		
Distilled water	81.28	81.28
Methylparaben	0.20	0.20
Butylene glycol	1.00	1.00
Glycerin	5.00	5.00
Arginine	0.20	0.20
Part B		
Cetyl alcohol	1.00	1.00
Butylparaben	0.10	0.10
Tocopheryl acetate	0.30	0.30
Phenoxyethanol	0.50	0.50
Part C		
Dimethicone	2.00	2.00
Cyclotetrasiloxane/Cyclohexasiloxane	1.00	1.00
PEG/PPG-18/18 Dimethicone	0.10	0.10
Cyclopentasiloxane	1.00	1.00
Part D		
Sodium hyaluronate	1.00	1.00
Carbomer	5.00	5.00
Part E		
3- <i>O</i> -Ethyl ascorbic acid	0.30	0.30
Part F		
Taxifolin tetra-octanoate	0.02	
Taxifolin		0.02

The formulas for taxifolin and taxifolin tetra-octanoate lotions are listed in Table 2. The lotions were prepared by heating part A to 80°C until dissolved. Part B was added to part A while homogenizing at a rate of 3000 rpm for 3 min. Subsequently, part C was added and emulsified under the same condition. Whereafter parts D, E and F were added together at stirring speed of 3000 rpm for 3 min and then reduced to 1500 rpm for 3 min. The lotions were then cooled with ice water and stirred at 500 rpm until room temperature was reached, and finally degassed.

Table 3. Components of the Essence Formulations under Study

Components	Percentage of components in each formulation (w/w)	
	F5	F6
Part A		
Distilled water	92.58	92.58
Methylparaben	0.20	0.20
Butylene glycol	0.50	0.50
Glycerin	1.00	1.00
Arginine	0.20	0.20
Part B		
Cetyl alcohol	0.10	0.10
Butylparaben	0.10	0.10
Tocopheryl acetate	0.30	0.30
Phenoxyethanol	0.50	0.50
Part C		
Dimethicone	0.50	0.50
Cyclotetrasiloxane/Cyclohexasiloxane	1.00	1.00
Part D		
Carbomer	3.00	3.00
Part E		
Taxifolin tetra-octanoate	0.02	
Taxifolin		0.02

The formulations for the taxifolin and taxifolin tetra-octanoate essences are given in Table 3. The compositions of part A were mixed together and heated to 80°C until dissolved. Then part B was added to part A while homogenization of different parts was achieved at stirring speed of 3000rpm. After 3min, part C was added with continuous stirring and emulsified under the same condition. Then part D was added ahead of part E. After all the components have been added, stirring was continued at a rate of 3000rpm for 3min and then reduced to 1500rpm for 3min. When the temperature dropped to room temperature, the essences were continuously stirred at 500rpm for 3min, and finally degassed.

Stability Evaluation of Formulations Formulations containing taxifolin and taxifolin tetra-octanoate were stored in a thermostat (Grant Instruments Ltd., Cambridge, U.K.) at 25 and 40°C with 75% relative humidity (RH) for up to 12 weeks, respectively. Formulations were evaluated for various parameters at the time intervals of 0, 1, 2, 4, 8 and 12 weeks.

Viscosity Measurement The viscosity of various formulations was determined at 0, 1, 2, 4, 8 and 12 weeks with a Brookfield viscometer (LVDV-II viscometer, Brookfield Engineering Laboratories, Inc., U.S.A.) fitted with No. 4 spindle. The product temperature to be tested was controlled by a Brookfield circulating water bath with a temperature controller (Massachusetts, U.S.A.). The viscosity of the formulations was determined at a stable temperature of 25°C. An amount of 100g of the product was placed into a glass container for viscosity reading. In each reading, the viscosity readings were taken every 1min during 10min.

pH Determination The pH of a formulation may influence the stability of active components in the formulation. In this study, the pH of each sample kept in different storage conditions was determined by a portable pH meter (LAQUAact, D-71, Horiba, Ltd., Japan). The samples of cream and lotion formulations were diluted to 1:15 (w/w) in distilled water. In the case of the essences, measurements were made at

their original concentrations. The pH of each formulation was determined at room temperature, right after the preparation and during the 12 weeks of the stability study. To ensure accuracy, three measurements were taken on each batch.

HPLC Analysis HPLC analysis was performed to measure the concentration of the formulations containing taxifolin and taxifolin tetra-octanoate at 0, 1, 2, 4, 8 and 12 weeks of stability testing. The HPLC analysis was performed by using an Agilent 1100 Series HPLC system, equipped with an Agilent 1100 pump, UV detector and autosampler. The data were acquired by ChemStation software, Rev.A.10.02 (Agilent Technologies, Palo Alto, CA, U.S.A.). A Luna C18 column (250×4.60mm, 5μm) was used for the content analysis of taxifolin, and a Brownlee Choice C18 column (100×2.1mm, 5μm) was used to analysis the content of taxifolin tetra-octanoate.

For the content analysis of taxifolin in all formulated products, degassed acetonitrile-1% acetic acid in water (30:70, v/v) was the mobile phase at a flow rate of 1.0mL/min. The injection volume was 10μL and analyse was performed at 280nm. One gram of formulation sample was transferred to a 20mL volumetric flask and diluted with methanol. Then, the samples were dissolved ultrasonically and filled to volume in the volumetric flask. The solution was filtered with a 0.20μm polytetrafluoroethylene (PTFE) membrane syringe filter and used for HPLC analysis.

The content analysis of taxifolin tetra-octanoate was different from the above, the mobile phase was a mixture of distilled water and acetonitrile (2:98, v/v). The flow rate was set to 1.0mL/min, and the sample injection volume was 20μL. The quantitative wavelength was set at 280nm. The samples were prepared by weighing 1g of each formulation into a 10mL volumetric flask and diluted with acetonitrile. The samples were sonicated until completely dispersed, and then were filled to volume in the volumetric flask after they were cooled to room temperature. All samples were filtered with a 0.20μm PTFE membrane syringe filter and transferred into HPLC vials for analysis. The studied compositions were quantified by using the calibration curves prepared from the standards.

Statistical Analysis The data are expressed as the mean ± standard deviation (S.D.) Statistical comparisons were made by one-way ANOVA using IBM SPSS software (IBM, U.S.A.), version 16.0. $p < 0.05$ was considered as statistically significant.

Results and Discussion

Currently, skin care formulations, such as cream, lotion, and essence, often use natural bioflavonoids including taxifolin as antioxidative and whitening components. However, because the weak stability of taxifolin greatly restricts its bioavailability and efficiency, it is necessary to synthesize taxifolin derivatives and further measure its stability. Hydroxyl groups on flavonoids are both crucial for the biological activities and key positions for further modification. Acylated flavonoids are relatively new substances and which have been reported to have significantly different biological, biochemical and biophysical properties.^{27–30} In general, researchers agree that the introduction of more lipophilic substituents on hydroxyl groups will improve the bioactivity and stability of polyhydroxy compounds. Tewtrakul *et al.* investigated seven methoxyflavone derivatives from *Kaempferia parviflora*, the results indicated

5-hydroxy-3,7,3',4'-tetramethoxyflavone possessed the highest anti-allergic activity.³¹⁾ Shi *et al.* synthesized 3,7,3',4'-tetramethoxyflavone and confirmed its acetylcholinesterase inhibitory activity.³²⁾ On the other hand, some studies indicated that octanoylated flavonoids exert better biological activity.^{33–35)} Therefore, we chose to synthesize 3,7,3',4'-tetra-octanoyltaxifolin in the present study and investigated the stabilities of it in different skin care formulations.

Effect of Taxifolin Tetra-octanoate on Tyrosinase Activity in Cell-Free System As tyrosinase is known to be the rate-limiting enzyme responsible for melanin biosynthesis, inhibitory effect of taxifolin tetra-octanoate on the activity of mushroom tyrosinase was investigated by using L-DOPA as the substrate in a cell-free system. The tyrosinase inhibitory activity is shown in Fig. 2. Results showed that taxifolin tetra-octanoate exhibited dose-dependent inhibition (24–63%) of tyrosinase activity at 1–50 $\mu\text{g/mL}$. Our results indicate that taxifolin tetra-octanoate possesses higher inhibitory effect on tyrosinase compared with taxifolin. This result is presumably due to the structure of tyrosinase, inside the structure, there are dinuclear copper in the active center of the enzyme and a lipophilic long-narrow gorge near to the active site. The ester group structure of taxifolin tetra-octanoate might show strong affinity toward dinuclear copper in the active site. There are similar presumptions in other literatures investigating tyrosinase inhibitors.^{36,37)}

In this study, six formulations were attained and designated F1 to F6. The formulations of F1 and F2 were creams; F3 and F4, lotions; and F5 and F6, essences. The major composition in F1, F3 and F5 was taxifolin tetra-octanoate; and in F2, F4 and F6, taxifolin. Nearly all of the currently existing formulations containing taxifolin or other flavonoids are based on the similar formulas for advanced lotion, essence, and cream. As a concentration of 0.001–0.1% (w/w) taxifolin has been used for a cosmetic formulation in the United States patent,³⁸⁾ we added 0.02% (w/w) taxifolin or taxifolin tetra-octanoate to different formulations, respectively. All of the formulations were stored for 12 weeks at 25 and 40°C, and measured the parameters of viscosity, pH and content at 0, 1, 2, 4, 8 and 12 weeks.

Fig. 2. Effect of Taxifolin Tetra-octanoate on Mushroom Tyrosinase Activity

Different concentrations of taxifolin tetra-octanoate were used to measure the tyrosinase inhibitory activity in a cell-free system. Data are presented as the mean $\pm$ S.D. of three independent measurements. ** $p < 0.01$ as compared to control.

Variations in Viscosity of the Cream, Lotion and Essence Formulations The formulation viscosity, a very important parameter for cosmetic application, can be measured by using rheological methods. These methods can be applied to the primary as well as the final cream, lotion and essence formulations.

According to the results of viscosity (Fig. 3), the obvious decreases in the viscosity of formulations containing taxifolin (F2, F4 and F6) can be found. Comparing the initial viscosities of formulaions F2, F4 and F6 with their viscosities after

Fig. 3. Variations in Viscosity of the Formulations

(a) Cream, (b) lotion and (c) essence. All of the formulations were stored for 1, 2, 4, 8 and 12 weeks at 25 and 40°C.

12 weeks of storage at 25°C, the viscosities decreased with approximately 378, 198 and 305 cP, respectively. The decreases in the viscosity at 40°C were a little more than those at 25°C, and they showed the variations of 404, 216 and 309 cP, respectively. Whereas the viscosities of each formulation containing taxifolin tetra-octanoate (F1, F3 and F5) did not exhibit significant variations over time at 25°C, they showed the decreases of 6, 9 and 6 cP, respectively. The variations in viscosity at 40°C were also similar to those at 25°C. The results showed that the viscosities of formulations containing taxifolin tetra-octanoate were relatively stable at different temperatures and storage durations.

The rheological study may obtain an evaluation of the physical properties and the structural stability of different formulations.³⁹⁾ The main factors affecting formulation viscosity are pH value, the concentration of polyvalent cation and Surfactant.^{40,41)} As the viscosity of formulation will decline along with the decrease of the concentration of the polyvalent cation, the metal chelation capacity of taxifolin may affect the formulation viscosity.⁴²⁾ In addition, because the phenolic hydroxyl groups of taxifolin are likely to be oxidized, the influence of oxidative products on pH value may be the factor affecting the viscosity.

pH Changes in the Cream, Lotion and Essence Formulations Detecting the pH change in cosmetic formulation is very important because the pH value will decide if the formulation is appropriate for topical use. The results in Fig. 4 showed the pH changes of the formulations stored at different temperatures for 12 weeks. The formulations F2, F4 and F6 showed a significant decrease in pH value compared with the formulations F1, F3 and F5. The changes in pH value at 25°C were within the ranges of 6.45–6.17, 6.27–5.99 and 6.24–5.92, respectively. The changes of formulations F2 and F4 at 40°C were more than those at 25°C, whereas the change of formulation F6 was similar to it at 25°C, they showed the changes of 6.45–5.98, 6.27–5.89 and 6.24–5.91, respectively.

The pH values of each formulation containing taxifolin tetra-octanoate (F1, F3 and F5) did not exhibit a significant change over time at 25°C, they showed minimal changes within the range of 6.43–6.38, 6.31–6.25 and 6.27–6.17, respectively. The changes of formulations F1 and F3 at 40°C were more than those at 25°C, whereas the change of formulation F5 was similar to it at 25°C, they showed the changes of 6.43–6.25, 6.31–6.14 and 6.27–6.16, respectively. The smallest pH change was observed in formulation F1 stored at 25°C. The results showed that the pH value of the formulations containing taxifolin tetra-octanoate is relatively stable at different temperatures and storage durations.

Previous studies revealed that pH values in the range of 5.5–6.5 are considered to be skin-friendly.⁴³⁾ Results of pH determination indicate that the variations in pH values of different formulations containing taxifolin tetra-octanoate can meet the requirement for skin application. The small changes in pH value detected may be due to the ester bonds hydrolysis which lead to generate acidic byproducts as reported in the similar work.⁴⁴⁾ The relatively obvious changes in pH value of formulations containing taxifolin were determined, these changes may be caused by the oxidation of phenolic hydroxyl groups of taxifolin.^{18,45)}

Chemical Stability of the Formulations HPLC method with UV detection was developed to determine the chemical

Fig. 4. pH Changes in the Formulations

(a) Cream, (b) lotion and (c) essence. Each formulation was stored for 1, 2, 4, 8 and 12 weeks at 25 and 40°C.

stability of formulations included in the study. The method is an ordinary procedure used in the quantitative and qualitative analysis of drugs and cosmetics.⁴⁶⁾

The storage stability of taxifolin and taxifolin tetra-octanoate presented in the formulations is shown in Fig. 5. Among the six studied formulations, taxifolin was highly unstable, both at 25 and 40°C during the storage period. Taxifolin in the formulations F2, F4 and F6 was found to decrease to

Fig. 5. Content Changes of the Major Active Components (the Initial Content Was Considered as 100%), Taxifolin and Taxifolin Tetra-octanoate (TTO), Presented in the Formulations

(a) Cream, (b) lotion and (c) essence. All of the formulations were stored for 1, 2, 4, 8 and 12 weeks at different temperatures (25 and 40°C).

approximately 12, 40 and 8% of the initial content at 25°C, respectively. The minimum amount of taxifolin was found in the formulation F6 stored at 40°C for 12 weeks, about 3% of the initial content.

Comparing different formulations, the stability of taxifolin tetra-octanoate in cream and lotion was higher than in essence

Fig. 6. Content Changes of Taxifolin Tetra-octanoate (TTO) in Each Formulation Stored for 1, 2, 4, 8 and 12 Weeks at Different Temperatures (a) 25°C and (b) 40°C. The initial content was considered as 100%.

formulation (Fig. 6). When the formulations F1, F3 and F5 were stored at 25°C for 12 weeks, the percentage of remaining taxifolin tetra-octanoate were about 93, 87 and 38%, respectively. During storage at 40°C for 12 weeks, the contents of remaining taxifolin tetra-octanoate were about 85, 83 and 20%, respectively. Only a minimum amount of taxifolin tetra-octanoate remained in the essence formulation after storage for 12 weeks, this was probably due to the conspicuously high levels of water in the aqueous solution, which accelerated hydrolysis reaction.^{47,48)} In addition, considering other components of the essence formulation, the most important element influencing the stability of taxifolin tetra-octanoate is the surfactant constituents, which may cause deprotonation influence in solution.⁴⁹⁾ The reason for the greater degradation of taxifolin tetra-octanoate in the essence formulation is not entirely clear, however, it is suggested that cream and lotion are more suitable as stable formulations for taxifolin tetra-octanoate, especially the cream (Fig. 6).

Conclusion

The stability of cream, lotion and essence formulations containing 0.02% taxifolin tetra-octanoate was studied during 12

weeks of storage at 25 and 40°C, and compared with the formulations containing 0.02% taxifolin at the same conditions. Our study demonstrated that formulations containing taxifolin tetra-octanoate showed better physical and chemical stability than other formulations. The results showed that storage time had no significant influence on the viscosity of formulations containing taxifolin tetra-octanoate. The pH changes were also smaller than that in the formulations containing taxifolin, the pH value was within the limits of normal skin pH range.

From the chemical stability studies, we can discover taxifolin tetra-octanoate in the essence formulation was most unstable at 25 and 40°C with about 62 and 81% degradation in 12 weeks of storage. It was concluded that cream formulation was best for maintaining the stability of taxifolin tetra-octanoate. In view of the higher inhibitory effect of taxifolin tetra-octanoate on tyrosinase activity compared with taxifolin in a cell-free system as well as the research results of formulation stability, it can be concluded that taxifolin tetra-octanoate has the potential to be developed as skin care products with better stability, such as cosmeceuticals.

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Conflict of Interest The authors declare no conflict of interest.

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