

1-1-2013

## COSMECEUTICAL DEVELOPMENT OF OXYRESVERATROL FROM MAHAD (ARTOCARPUS LAKOOCHA ROXB.)

Surapol Natakankitkul

Nicha Chareonmuang

Tawan Panyakhong

Worrapon Wangkananon

Follow this and additional works at: <https://digital.car.chula.ac.th/tjps>

 Part of the [Pharmacology Commons](#)

---

### Recommended Citation

Natakankitkul, Surapol; Chareonmuang, Nicha; Panyakhong, Tawan; and Wangkananon, Worrapon (2013) "COSMECEUTICAL DEVELOPMENT OF OXYRESVERATROL FROM MAHAD (ARTOCARPUS LAKOOCHA ROXB.)," *The Thai Journal of Pharmaceutical Sciences*: Vol. 38: Iss. 0, Article 62.  
Available at: <https://digital.car.chula.ac.th/tjps/vol38/iss0/62>

This Article is brought to you for free and open access by the Chulalongkorn Journal Online (CUJO) at Chula Digital Collections. It has been accepted for inclusion in The Thai Journal of Pharmaceutical Sciences by an authorized editor of Chula Digital Collections. For more information, please contact [ChulaDC@car.chula.ac.th](mailto:ChulaDC@car.chula.ac.th).

**COSMECEUTICAL DEVELOPMENT OF OXYRESVERATROL FROM MAHAD  
(*ARTOCARPUS LAKOOCHA* ROXB.)**

Surapol Natakankitkul<sup>1</sup>, Nicha Chareonmuang<sup>1</sup>, Tawan Panyakhong<sup>1</sup> and Worrapon Wangkananon<sup>2</sup>

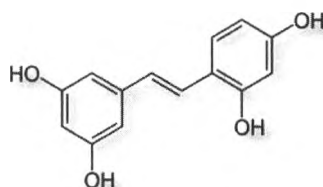
<sup>1</sup>Department of Pharmaceutical Science, Faculty of Pharmacy, Chiang Mai University, Chiang Mai, Thailand.

<sup>2</sup>Mintech Laboratory Co. Ltd, 199/273 Soi Choet Wutthakat 9, Don Muang, 10210 Bangkok, Thailand.

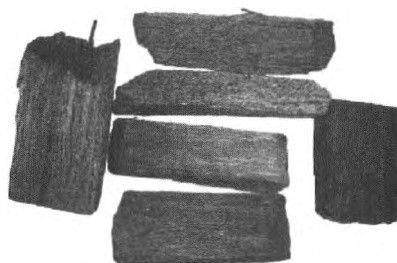
**KEYWORDS:** Oxyresveratrol, Skin whitening, Mahad, *Artocarpus lakoocha* Roxb.

**INTRODUCTION**

Oxyresveratrol (Figure 1), a natural phenolic stilbene compound found in Mahad (*Artocarpus lakoocha* Roxb.) heartwood extract, exhibited a potent inhibitory effect on tyrosinase enzyme which catalyzes rate-limiting steps in biosynthesizing human melanin pigment [1,2]. In Thailand, herbal cosmetics are becoming more popular especially for nourishing and whitening skin. Several plant extracts were found to exhibit strong anti-tyrosinase activity *in vitro* such as those from *Areca catechu* L. [3], *Artocarpus incisus* [4], *Broussonetia* spp. (paper mulberry root bark extract) [5], *Glycyrrhiza glabra* (licorice extract) [6], *Prunus* spp. [7], and *Rheum officinale* [8]. Many of these extracts have been tested *in vivo* and commercially developed as skin whitening agents in cosmetic preparations such as *Morus alba* and licorice extracts [9,10]. However, they are quite expensive and some users may develop skin hypersensitivity especially when applying them at high concentrations. Some preliminary studies were developed skin-whitening solution containing Mahad heartwood extract which had oxyresveratrol as the active ingredient [11,12]. The main objective of this study was therefore to study the extraction process and the properties of Mahad extract and measured the amount of oxyresveratrol in the extract, developed lotion formulation from Mahad extract, clinical evaluated whitening skin and investigated the satisfaction of using Mahad lotion in the female volunteers.



**Figure 1** Oxyresveratrol chemical structure.



**Figure 2** The dried wood chips of heartwood Mahad (*Artocarpus lakoocha* Roxb.).

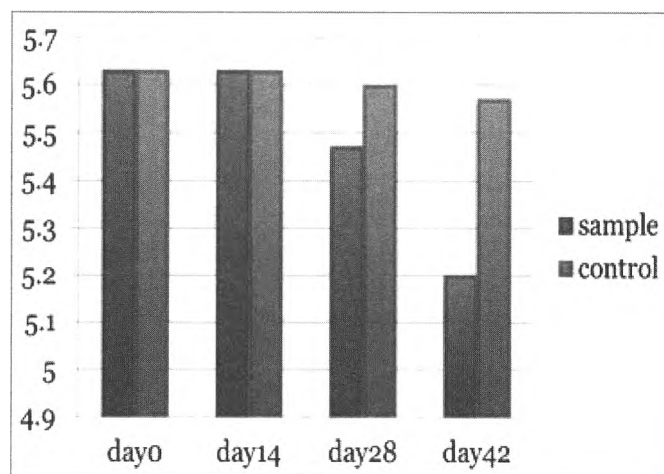
## MATERIALS AND METHODS

**Materials** Oxyresveratrol was donated from Youcandu Institute. Mahad (*Artocarpus lakoocha* Roxb.) heartwood was received from Mintech Laboratory Factory. All other reagents were of analytical and HPLC grade.

**Methods** The dried wood chips of heartwood Mahad (Figure 2) was continuously extracted with ethanol using Soxhlet apparatus (40 mm ID extractor, with 500-mL round bottom flask) and slow alcohol evaporation by Rotavapor (BÜCHI Labortechnik AG, Switzerland). Then the extract was identified as oxyresveratrol by TLC (Silica gel 60 GF254 plates and developing solvent of chloroform: methanol = 9:1 v/v) and UV-visible spectroscopy. The amount of oxyresveratrol in the extract was measured by HPLC. Chromatographic analyses used a Shimadzu prominence UFLC system (Shimadzu, Japan) connected with Hypersil ODS column (4.0x250 mm, 5-micron; Agilent, USA). The mobile phase consisted of acetonitrile and DI water with acetic acid (30:70:0.04 v/v). The flow rate of mobile phase was maintained at 1.0 ml/min. Sample injection volume was 10 µl. The UV detection for oxyresveratrol was carried out at 320 nm.

**Formulation and in vivo evaluation of lotion containing Mahad extract** The Mahad or *A. lakoocha* extract was formulated as an oil-in-water emulsion in 3 lotion formulations and selected the best physical and chemical properties of the formulation. The lotions containing Mahad extracts were also freshly prepared and used within 2 months. Additionally, the stability study; tyrosinase inhibitory activity, HPLC, colour and odour of the formulation kept by cooling and heating cycle (4, 45 °C; 48 hr) for 6 cycles were studied.

**In vivo evaluation of skin whitening activity of Mahad lotion** The protocol was approved by the Ethics Committee of the Faculty of Pharmaceutical Sciences, Chiang Mai University. Thirty female volunteers, age between 20 and 23 years with normal healthy skin, were recruited in the study. The *in vivo* physical-whitening activity was further evaluated in 30 female volunteers. The initial melanin values were taken from both the left and right lower arms of each subject using Mexameter MX16 (Courage and Khazaka, Germany) before application of the test lotions. The initial melanin values were tested between the left and the right arms within each subject to make sure that the starting melanin values were the same before product application ( $P > 0.05$ , paired *t*-test). The subjects were daily applied each her arm blindly with 1% w/v Mahad testing lotion and lotion base using a parallel clinical trial with self-control. The lotion then assessed the satisfaction of using lotion for 6 weeks. The score value of whitening was measured each application site of each arm every two weeks using skin-colors tone band then compared relative to the initial treated arms within the same subject using paired *t*-test ( $\alpha = 0.05$ ). All the experimental data were expressed as means  $\pm$  SD.



**Figure 3** The whitening activity in average skin-colors tone score after daily application to the lower arms of female volunteers for 6 weeks with 1% Mahad lotion (sample) in comparison with lotion base (control). Data = means  $\pm$  SD ( $n = 30$ ). Day42\* significantly greater than control ( $P < 0.05$ ) at the same week.

## RESULTS AND DISCUSSION

The results showed oxyresveratrol was the major active ingredient in the Mahad extract and the percent yield of extraction measured by HPLC was 35.13%w/v. The stability test of formulated lotion by cooling and heating of 6 cycles found that the test lotion was still stable with more viscous and pale color. While Pothitirat *et al.* [13] reported that the whitening skin lotion containing 1.03% of Mahad extract stored at 4°C for 4 weeks, the antityrosinase activity, TLC, colour and odour of the lotion were not changed. The percentage of tyrosinase inhibition of Mahad extract at concentration of 1 mg/mL was found to be  $87.88 \pm 0.31$  ( $IC_{50} = 50 \mu\text{g/mL}$ ) [14]. The melanin-reducing efficacy was also measured using Maxameter. The whitening activity of the selected lotion evaluated in female volunteers found that daily application with 1% Mahad lotion to the upper arms ( $n = 30$ ) of volunteers produced significant over the lotion base after 4 weeks. From Figure 3, it can be seen that the average skin-colors tone score for whitening activity of the lower arms treated with Mahad lotion continuously decreased with the treatment duration, i.e. from 2.84% at week 4 to 7.64% at week 6. During the same period, the values for the arms treated with lotion base (self-control) decreased only slightly from 0.53% at week 4 to 1.06% at week 6. When paired *t*-test was applied to the whitening data at various weeks, significant difference was found in the mean % whitening values between the arms treated with Mahad lotion and the self-control arms after 4 weeks of application. After week 4, the significance became even more pronounced ( $p < 0.05$ ) as the difference between the two arms continued to increase until the end of the study (week 6), indicating a greater whitening efficacy of Mahad lotion over the control. The oxyresveratrol was the most effective agent giving the short onset of significant whitening effect after only day 28 of application ( $p < 0.05$ ). The effect also increased with time with maximum whitening observed at day 42 after applied lotion significantly ( $p < 0.05$ ). However, more studies are needed to confirm the clinical efficacy and safety of the Mahad extract in larger panel of subjects using different formulations and/or in combination with other whitening agents.

Recently, Sritularak *et al.* [15] have screened a large number of plants for their *in vitro* anti-tyrosinase activity and found that the heartwood extract of *A. lakoocha* exhibited the highest activity. Purification of the extract yielded two active components, namely oxyresveratrol and resveratrol. Comparing to other tyrosinase inhibitors commonly used in whitening products like kojic acid and licorice extract, the readily available and less expensive *A. lakoocha* extract apparently produced a faster onset of significant whitening effect, requiring only 2–4 weeks of application depending on the type of formulation and area of application. The greater anti-tyrosinase activity of oxyresveratrol (tetrahydroxystilbene derivative) was probably due to its higher number of phenolic hydroxy substituents, whereas resveratrol is a trihydroxy analogue. It has been suggested that the number and position of phenolic hydroxy groups and the presence of *trans*-olefin structure in the stilbene derivatives play an important role in their enzyme inhibitory potencies [9,16].

The oil-in-water emulsion appeared to provide better whitening activity than the lotion base. The mild skin whitening effect of Mahad extract could be considered a desirable attribute for use in cosmetic preparations as its whitening activity will be gradual and more natural. However suitable UV filters/absorber or sun-screening agents should be included in future formulations to enhance their whitening efficacy. Regarding the side effects, no skin rashes or serious skin disorders were observed in all subjects receiving the test lotion. Considering the low concentrations employed in this study (1%), the extract may have a very promising potential for use as a safe, effective and economical whitening agent in the cosmetic industry. The overall satisfactions of using Mahad lotion in the volunteers were in moderate to good level.

## CONCLUSION

The results of the studies demonstrated that the heartwood Mahad or *A. lakoocha* extract lotion was able to reduce melanin formation in human volunteers have a promising potential for use as an effective and economical skin-whitening cosmeceutical.

## REFERENCES

1. Jagtap UB and Bapat VA. 2010. *Artocarpus* : A review of its traditional uses, phytochemistry and pharmacology. J Ethnopharmacol 129: 142-166.
2. Chang TS. 2009. An Updated Review of Tyrosinase Inhibitors. IJMS 10: 2440-2475.
3. Lee KK and Choi JD. 1999. The effect of *Areca catechu* L. extract on anti-inflammatory and antimelanogenesis. Int J Cosmet Sci 21: 275-284.
4. Shimizu K, Kondo R, Sakai K, Lee SH and Sato H. 1998. The inhibitory components from *Artocarpus incisus* on melanin biosynthesis. Planta Med 64: 408-412.
5. Jang DI, Lee BG, Jeon CO. et al. 1997. Melanogenesis inhibitor from paper mulberry. Cosmetics Toiletries 112: 59-62.
6. Yokota T, Nishio H. and Kubota Y. 1998. The inhibitory effect of glabridin from licorice extracts on melanogenesis and inflammation. Pigment Cell Res 11: 335-361.
7. Matsuda H, Nakamura S and Kubo M. 1994. Studies of cuticle drugs from natural sources. II. Inhibitory effects of prunus plants on melanin biosynthesis. Biol Pharm Bull 17: 1417-1420.
8. Iida K, Hase K, Shimomura K, Sudo S, Kadota S and Namba T. 1995. Potent inhibitors of tyrosinase activity and melanin biosynthesis from *Rheum officinale*. Planta Med 61: 425-428.
9. Kim JH and Lee KT. 1998. Inhibitory effects of *Morus alba* extracts on melanogenesis. Cosmetics Toiletries 113: 65-70.
10. Petit L and Piérard GE. 2003. Skin-lightening products revisited. Int J Cosmet Sci 25: 169-181.
11. Zheng ZP, Cheng KV, To JT, Li H, Wang M. 2008. Isolation of tyrosinase inhibitors from *Artocarpus heterophyllus* and use of its extract as antibrowning agent. Mol Nutr Food Res 52(12): 1530-1538.
12. Likhitwitayawuid K and Sritularak B. 2001. A New Dimeric Stilbene with Tyrosinase Inhibitory Activity from *Artocarpus gomezianus*. J Nat Prod 64(11): 1457-1459.
13. Pothitirat W, Pluemlamai J, Satniyom S, Leelamanitaya W, Gritsanapan W. 2010. Development of whitening skin lotion from selected medicinal plants and its antityrosinase activity. Planta Med 76: 174.
14. Tengamnuay P, Pengrungruangwong K, Pheansri I, Likhitwitayawuid K. 2006. *Artocarpus lakoocha* heartwood extract as a novel cosmetic ingredient: evaluation of the in vitro anti-tyrosinase and in vivo skin whitening activities. Int J Cosmet Sci 28(4): 269-276.
15. Sritularak B, De-Eknamkul W and Likhitwitayawuid K. 1998. Tyrosinase inhibitors from *Artocarpus lakoocha*. Thai J Pharm Sci 22:149-155.
16. Ohguchi K, Tanaka T, Kido T. et al. 2003. Effects of hydroxystilbene derivatives on tyrosinase activity. Biochem Biophys Res Commun 307:, 861-863.