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Napa Bunma

Jirapan Moungjaroen

Prasan Tanguenyongwatana

DEVELOPMENT OF *GARCINIA MANGOSTANA* EXTRACT IN LIQUID CRYSTAL CREAM FOR TOPICAL DELIVERY SYSTEM

Napa Bunma[1], Jirapan Moungjaroen[2], Prasan Tanguenyongwatana[1,*]

[1]*Faculty of Oriental Medicine, Rangsit University, Pathumthani 12000, Thailand*
[2]*Numsiang International CO. LTD. 19 Sukumvit 70, Bangna, Bangkok 10260, Thailand*

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INTRODUCTION

Garcinia mangostana L. is a medicinal plant that has long history in medicinal use in Southeast Asia for treatment of diarrhea, skin infection and chronic wounds[1]. The extract of its pericarp has demonstrated antibacterial activity against many types of microorganism[2, 3]. The ethanol extract of mangosteen fruit rinds was also active against *Propionibacterium acnes* and *Staphylococcus epidermis* with MIC of 7.81 and 15.63 µg/mL, respectively[4]. Currently, liquid crystal systems are used to modify drug delivery system for the delivery of topical drugs into skin[5]. Liquid crystals are highly anisotropic fluids that exist as a result of long-range orientation ordering among constituent molecules. They are also three-dimensional association structures that stabilize emulsions[6]. Our objective is to develop a liquid crystal cream containing *G. mangostana* fruit rind extract to be used as a topical anti-acne product.

MATERIALS AND METHODS

Instrument and reagents 1, 3-Butylene glycol was purchased from Kyowa Hakko (Tokyo, Japan). Carbopol ultrez polymer was purchased from Lubrizol (Ohio, USA). L-Arginine was purchased from CellMark (Balmoral Plaza, Singapore). NIKKOMULESE LC was purchased from Nikkol (Tokyo, Japan). Cetostearyl alcohol and caprylic/capric triglyceride were purchased from Parchem (New York, USA). The polarized light microscopy was performed on a Nikon Eclipse 50i POL (Tokyo, Japan). Viscosity measurement was performed using a Fungilab VISCOSTAR plus viscometer (Barcelona, Spain). All other reagents and solvents were reagent grade and used without further purification. TLC was performed on silica gel GF_{254} plates (Merck). For column chromatography, silica gel (Merck 230-400 mesh) was used. NMR spectra were recorded with a Bruker Avance (300 MHz) spectrometer. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. All NMR spectra were obtained in deuterated chloroform ($CDCl_3$) and referenced to the residual solvent peak. Mass spectra were obtained from an Agilent GC/MS 5975C.

Plant material The fruit rinds of *G. mangostana* were bought from local drugstore in Nonthaburi province, Thailand. The material was identified by comparison with the specimen at the Forest Herbarium, Department of National Park, Wildlife and Plant Conservation, Ministry of Natural Resources and Environment, Bangkok. The voucher specimen of *G. mangostana* (SRU 026) was deposited at the Faculty of Oriental Medicine, Rangsit University, Pathumthani, Thailand.

Preparation of crude and partially-purified extracts The dried, powdered fruit rinds of *G. mangostana* (100 g) were extracted with 95% ethanol (400 mL) at room temperature for 7 days. The extract was filtered with Whatman No.1 filter paper and then evaporated under reduced pressure to obtain 9 g of crude dark brown extract. The crude extract (2 g) was dissolved in CH_2Cl_2-MeOH (8:2) (8 ml). The mixture was then subjected to silica gel column chromatography, eluted with CH_2Cl_2-MeOH (8:2), to obtain partially purified dark brown extract (1.2 g).

Isolation of α-mangostin The crude extract (1.2 g) was dissolved in 5 ml of CH_2Cl_2-MeOH (7:3), then subjected to silica gel column chromatography eluted with CH_2Cl_2-MeOH (7:3) as the mobile phase. After that, fractions 12-17 were collected and evaporated to obtain a yellow crystalline solid (212 mg) with melting point of 180-182 °C. UV [7] λ_{max} 244, 343 nm; IR [8] (KBr disc): 3256, 2925, 1639, 1460 cm^{-1}; ^1H NMR [9] (300 MHz, $CDCl_3$) δ [ppm]: 1.69 (s, 4H), 1.76 (s, 3H), 1.83 (s, 6H), 3.45 (d, J = 7.15 Hz, 2H), 3.81 (s, 3H), 4.09 (d, J = 6.26 Hz, 2H), 5.26 (m, 2H), 6.29 (s, 1H), 6.82 (s, 1H), 13.77 (s, 1H). ^{13}C NMR [9] (75 MHz, $CDCl_3$) δ [ppm]: 182.0, 161.6, 160.6, 155.8, 155.0, 154.5, 142.5, 137.0, 135.7, 132.2, 123.1, 121.4, 112.2, 108.5, 103.6, 101.6, 93.3, 62.0, 26.5, 25.8, 25.8, 21.4, 18.2, 17.9 and MS [9] (GC/MS): M^+ = 410.

Preparation of G. mangostana liquid crystal cream The *G. mangostana* liquid crystal cream was prepared as o/w emulsion cream. The process started with using NIKKOMULESSE LC, cetostearyl alcohol, caprylic/capric triglyceride and *G. mangostana* partially purified extract (0.1% w/w) as oil phase adding into 1,3-butylene glycol, Carbopol ultrez, L-arginine and water at 80 °C. The mixture was

homogenized and left to cool down to 50 °C before DM DM Hydantoin was added and mixed together. The product was evaluated with polarized light microscopy.

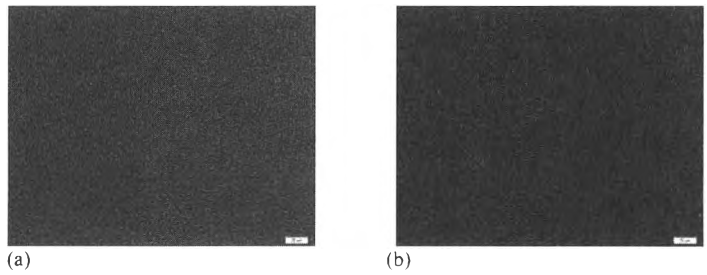
Table 1 Composition of liquid crystal cream ingredients

No.	Name of chemicals	% w/w
1	Water	71.4
2	1,3-Butylene glycol	5.0
3	Carbopol ultrez	0.1
4	NIKKOMULESSE LC	5.0
5	Cetostearyl alcohol	3.0
6	Caprylic/capric triglyceride	15.0
7	L-Arginine	0.1
8	DM DM Hydantoin	0.3
9	*Garcinia mangostana* partially purified extract	0.1

RESULTS AND DISCUSSION

The purification of *G. mangostana* crude extract with silica gel column chromatography to partially purified extract was uncomplicated process and could dispose of undesirable components that give unwanted color to the product. The partially purified extract of *G. mangostana* was standardized for α-mangostin by using HPTLC.

For the preparation of *G. mangostana* liquid crystal cream, the thermotropic method was chosen to make liquid crystals. In this formula, NIKKOMULESSE LC, which composed of cetyl alcohol, stearyl alcohol, behenyl alcohol, phytosterol, glyceryl stearate, carprylic/capric triglyceride, hydrogenated lecithin, and PEG-20 phytosterol, performed a major role in forming liquid crystal. After homogenized and cooled down to room temperature, the viscous emulsion became nicely smooth, yellow cream with viscosity of 58,365 cP. We smeared a small amount of cream onto a glass slide and examined it with a polarized light microscope (Figure 1). The first image (a) showed smooth texture of the emulsion droplets of the cream base while the *G. mangostana* cream (b) showed droplets of slightly bigger size.



(a) (b)

Figure 1 Picture of cream base (a) *G. mangostana* cream (b) under light microscopy.

Liquid crystals are highly anisotropic fluids and their three-dimensional association structures stabilize the emulsions. The dualism between a solid (crystal) and a flowing liquid gives rise to the term liquid crystal. Their structure has the ability to bend/refract and reflect polarized light such that they exhibit birefringence under the microscope [6, 10].

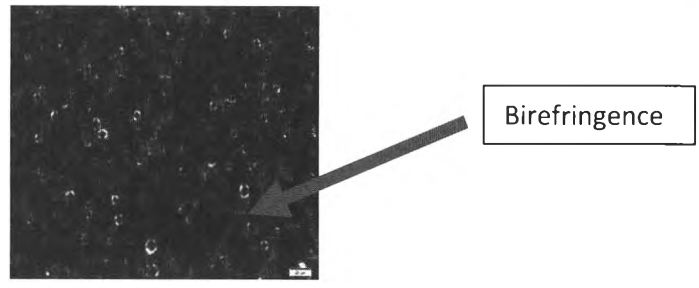


Figure 2 Liquid crystals of *G. mangostana* cream, when viewed under a polarized light microscope, showed the birefringence.

Figure 2 showed droplets of *G. mangostana* extract emulsion surrounded by a highly structured lamellar liquid crystalline gel network acting to reduce the likelihood of particle coalescence. This photomicrograph clearly shows the birefringence, which is the hallmark of liquid crystals surrounding emulsion droplets.

CONCLUSION

From our study, the formation of *G. mangostana* extract into liquid crystal form is easy with the help of a specific ingredient, NIKKOMULESSE LC. The way to prove the formation of liquid crystals is also easily done by observing the birefringence under polarized light microscope. This mixture of emulsifiers can create a lamellar structure that responsible for delivery the active ingredients into the skin. This liquid crystal form can enhance the absorption of active compounds through the skin. This formula can be applied to develop other medicinal plants for cosmetic and medicinal purposes.

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