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[AJPCR] Article Review Request

2 pesan

editor ajpcr <ajpcr@innovareacademics.in> 12 September 2019 14.27
Kepada: Muhammad Yanis Musdja <yanis.musdja@uinjkt.ac.id>

Muhammad Yanis Musdja:

I believe that you would serve as an excellent reviewer of the manuscript, "COMPARATIVE STUDIES ON PHYSICOCHEMICAL PROPERTIES OF MORINDA CITRILIA GEL AND OINTMENT FORMULATIONS," which has been submitted to Asian Journal of Pharmaceutical and Clinical Research. The submission's abstract is inserted below, and I hope that you will consider undertaking this important task for us.

Please log into the journal web site by 2019-09-26 to indicate whether you will undertake the review or not, as well as to access the submission and to record your review and recommendation.

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Thank you for considering this request.

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"COMPARATIVE STUDIES ON PHYSICOCHEMICAL PROPERTIES OF MORINDA CITRILIA GEL AND OINTMENT FORMULATIONS"

Abstract

Objective: The objective of this study is comparing the physicochemical properties of noni formulation in various conditions.

Methods: Methanolic fruit extracts of *Mrinda citrifolia* were used for the preparation of gel and ointment formulations that were evaluated for their phytochemicals and physicochemical, and stability at various conditions.

Results: Phytochemical screening studies of *Morinda citrifolia* revealed the presence of bioactive. In addition, evaluation for physical and chemical stability showed that gel formulation was more stable than ointment formulation.

Conclusion: Gel formulation could become a media to be used for its medicinal properties.

Dr. Yanis Musdja, M.Sc. <yanis.musdja@uinjkt.ac.id> 2 Oktober 2019 23.59
Kepada: editor ajpcr <ajpcr@innovareacademics.in>

Dear editor team

As attached, I send the results of my revision to the Title:

COMPARATIVE STUDIES ON PHYSICOCHEMICAL PROPERTIES OF MORINDA CITRILIA GEL AND OINTMENT FORMULATIONS

For this manuscript to be published in the Journal of Pharmaceutical and Clinical Research there must be improvements as I wrote in the attachment

Thank you very much for your attention and cooperation

Best Regards
Dr. Muhammad Yanis Musdja
[Kutipan teks disembunyikan]

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COMPARATIVE STUDIES ON PHYSICOCHEMICAL PROPERTIES OF *MORINDA CITRILIA* GEL AND OINTMENT FORMULATIONS

ABSTRACT

Objective: ~~*Morinda citrifolia* or noni is a herb that has been used traditionally. Recently, it attracted a great interest toward its application to be used as a herbal drug concomitant with modern medicine. It has an anti inflammatory, wound healing and other positive effects.~~ The objective of this study is comparing the physicochemical properties of noni formulation in various conditions ~~to get a phytochemical screening, formulation, and evaluation of physicochemical properties of *Morinda citrifolia* formulations~~.

Methods: Methanol~~ic~~ fruit extracts of *Mrinda citrifolia* were used for the preparation of gel and ointment formulations that~~. After completion of formulations, they~~ were evaluated for their phytochemicals and physicochemical~~,~~ ~~parameters such as color, odor, homogenous, physical appearance, pH, viscosity and bioactive~~ and ~~. Also, the formulations were evaluated for their~~ stability at various ~~temperature~~ conditions.

Results: Phytochemical screening studies of *Morinda citrifolia* revealed the presence of bioactive~~anthraquinone, cardiac glycosides, coumarins, tannins, alkaloids, phenols and flavonoids~~. In addition, evaluation for physical and chemical stability~~stability~~ showed that gel formulation was more stable than ointment formulation.

Conclusion: Gel formulation could become a media to be used for its medicinal properties.

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Keywords: *Morinda citrifolia*, ~~noni, gel,ointment,~~ phytochemicals, formulation, stability, scopoletin ~~phytochemicals parameters, high performance liquid chromatography~~

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INTRODUCTION

Herbal therapy has been used as a traditional medicine as well as in alternative medicine practiced in the developing countries. The widespread interest in a drugs derived from plants is because of the belief that plants are safe and dependable with less side effects. Review of literature revealed that traditional plant drugs are beneficial for several skin related problems and for wound healing ~~(Naira, 2010, Kumar *et al*., 2007, Strodtbeck, 2001)~~[1-3]. Thailand has been promoting the use of traditional medicine because they are less expensive, easily obtained and comprehensive, especially in developing countries ~~(Lokesh *et al*., 2017)~~[4]. Therefore, studies are searching for new drugs extracted from nature to be used for medicinal purposes which are less toxic and with no side effects unlike chemical drugs. At the present, people are more interested in the use of herbs for diseases treatment or to be used as a health food supplement. Therefore, the government has made a policy to support research and development of herbal medicines in order to add value to herbal drug products and to reduce importing drugs from abroad. In addition, it is also a career option for the labor which leads to improve the economy.

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Morinda citrifolia commonly known as "Noni" is a small tree native to South East Asia. It is also called as Indian Mulberry, Nono or Nonu, Cheese fruit, and Nhau in various cultures throughout the world. Components isolated from noni include scopoletin, octoanoic acid, potassium, vitamin C, terpenoides, alkaloids, anthroquinones, sitosterol, β-carotene, vitamin A, flavone glycosides and linoeic acid. The leaf contains flavanol glycosides, beta-carotene and iridoid glycosides

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~~(Levand and Larson, 1979)~~[5-6]. It is also reported to have a broad range of nutritional and therapeutic values for cancer, infection, arthritis, diabetes, asthma, hypertension and pain. It also has a muscle stimulatory and antihistamine effects along with antibacterial, antiviral, anti-tubercular, antitumor, anthelmintic, analgesic, hypotensive and immunological effects. Noni has been used as a traditional remedy to treat broken bones, deep cuts, bruises, sores and wounds ~~(Wang *et al*., 2002)~~[7]. The fresh leaf is used for wounds treatment and as a poultice for broken bones in most parts of India ~~(Yusliant *et alt*., 2013)~~[8]. Previous researches has shown that extracts from hexane ethanol and methanol of noni show wound healing capability by adding ligand binding to PDGF and A_{2A} receptors ~~(Afa *et alt*., 2010)~~[9]. Previous researches showed 10% topical morinda ethanol extract gel had a significant effect on rat skin excisional wound healing compared to 10% povidone iodine [10]. At the present, products from noni extract has various forms such as capsule, shampoo, soup and supplement but topical form not development that topical form, gel or ointment, detailed information regarding its wound healing capability are not completely documented. The objective of the current study is comparative studies on physicochemical properties of *Morinda citrifolia* gel and ointment formulations.

~~At the present, products from noni extract with detailed information regarding its wound healing capability are not scientifically documented. The objectives of the current study were is to get a phytochemical screening, formulation, and evaluation of physicochemical properties of *Morinda citrifolia* formulations. The stabilities of the gel formulation and ointment formulation were also compared.~~

~~MATERIALS AND~~ METHODS

Collection of Plant Materials

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Fruits of *Morinda citrifolia* were collected from Mahasarakham province, Thailand in October 2018. They were washed with distilled water, air dried and then made to fine powder with a mechanical grinder.

Extraction

About 1.6 kg of the powder sample~~ed plant~~ was suspended in 9 L of methanol on a hot plate (30 °C) for 24 hr. After extraction, the sample ~~that, the extract~~ was ~~the~~ filtered by using a fine muslin cloth followed by a filter paper (Whatman No. 1) and concentrated at 45 °C using rotary vacuum evaporator. The preliminary phytochemical screening was carried out by methanolic extract for the presence of phyto constituents ~~The extract was subjected to preliminary phytochemical analysis (Kokate *et al*., 1995, Evans, 2002)~~[11-12].

Phytochemical Screening Methods

Anthraquinone

The e~~E~~xtract (10 g) was boiled with 20 ml of 1% hydrochloric acid and 3% hydrogen peroxide 2 ml for 15 min. The extract was filtered and then waited until cooled. The extract was added to dichloromethane 10 ml and ammonium hydroxide 3 ml.~~; the mixture~~. Pink color of the base layer

indicates the presence of anthraquinone ~~(Panyarajun, 1996)~~[13].

Cardiac glycosides

The e~~E~~xtract (10 g) was boiled with 20 ml ethanol for 15 min. The mixture (5 ml) was ~~Five ml of the filtered were~~ placed in an evaporating dish and ~~then~~ evaporated to dryness. ~~; add to~~ Then 2% of 3, 5- D~~d~~initrobenzoic acid (Kedde reagent~~–~~) (1 ml)~~.~~ and 1 M of potassium

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hydroxide (0.5 ml) were added. Purple color -indicates the presence of cardiac [13].~~glycosides (Panyarajun, 1996).~~

Saponins

The ~~E~~extract (10 g) was boiled with 20 ml water for 15 min; the mixture was cooled and mixed vigorously and left for 3 min. The formation of frothing indicates the presence of saponins [13].~~(Panyarajun, 1996).~~

Coumarins

The e~~E~~xtract (2 g) was put into two tubes and~~were~~ covered by filter paper coated with water and sodium hydroxide, respectively and incubated into a

~~And then brought for a~~ water bath (37 ˚C) for ~~about~~ 5 min. Blue-green color on the filter paper coated with sodium hydroxide under ultraviolet light (366 nm) indicates the presence of coumarins [13].

~~(Panyarajun, 1996).~~

Tannins

The e~~E~~xtract (10 g) was boiled with 20 ml water for 15 min. Then 1~~One~~ ml of the solution was filtrate ~~ered~~ added to the 1 ml of 3% gelatin solution ~~1 ml; the mixture~~. Precipitation indicates the presence of tannins [13].~~(Panyarajun, 1996).~~

Flavonoids and phenolic content

The e~~E~~xtract (10 g) was boiled with 20 ml ethanol for 15 min. Then 1 ~~One~~ ml of the solution was ~~filtered~~ added to 1% ferric chloride.~~; the mixture.~~ Green-black color -indicates the presence of flavonoids [13].~~(Panyarajun, 1996).~~

Alkaloids

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The e~~E~~xtract (10 g) was boiled with 20 ml of 1% hydrochloric acid for 15 min. Then 10 ml of the solution was ~~filtered was~~ added to 10 ml of dichloromethane. ~~10 ml; the mixture~~. The extract ~~hen, 5 ml of the filtered~~ in dichloromethane layer (5 ml) was separated and added 2 drops of the ~~to using~~ alkaloid precipitating reagents. Precipitation more than 70% indicates the presence of alkaloids [13].

~~(Panyarajun, 1996).~~

Procedure for gel base and ointment base formulation preparation

Gel base formation

~~Dilutes~~ *Morinda citrifolia* fruit extract (10 g) was ~~with deionized water; mixture. That filtered was~~ mixed with 1 g of Carbopol ultrez ~~was dispersed~~ in 50 ml of deionized water. Then propylene glycol (1.5 g) and paraben (1.0 g) and triethanolamine (1.4 g) were added and mixed. ~~All the ingredients were mixed propylene glycol and paraben concentration~~. ~~Triethanolamine was added drop wise to the formulation for the adjustment of skin pH (5-6); mixed and~~ The final volume was made up to 100 ml by adding remaining distilled water, also to obtain a gel at the required consistency ~~(Avinash *et al*., 2016, Rajasree et al., 2012)~~[14-15]. Prepared gel was filled in a container and stored in a place avoiding light. The method described above and the formulae were tabulated in Table 1.

Ointment base formation

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Morinda citrifolia fruit extract (10 g) and white petrolatum (90 g) were mixed (geometric dilution). Prepared ointment was filled in a container and protected from light. The method described above and the formulae were tabulated in Table 2.

Table 1: Gel base formulation (10%)

Name of the ingredient	Quantity (g)	Properties of ingredient
Morinda citrifolia extract	10.0	Active ingredient
Carbopol ultrez®	1.0	Gelling agent
Propylene glycol	1.5	Humectant
Triethanolamine	1.4	pH adjusting agent
Paraben concentrate	1.0	Preservative
Deionized water	qs to 100.0	Vehicle

Table 2: Ointment base formulation (10%)

Name of the ingredient	Quantity (g)	Properties of ingredient
Morinda citrifolia extract	10.0	Active ingredient
White petrolatum	90.0	Ointment base

Evaluation of physicochemical properties of ~~topical~~ gel and ointment formulations

Physical stability test

Physical stability test of the formulations were carried out for 36 days by measuring in the initial (0 day) and second time (36 days ~~after~~). At various temperature conditions 1) ~~such as~~ room temperature ~~-~~ (25 ± 2°C), 2) cold ~~-~~(4°C) ~~-~~and 3) heating-cooling cycle (kept in hot oven at 45 ^{o}C for ~~about~~ 48 hours and kept in cold temperature 4°C for ~~about~~ 48 hours) ~~(Avinash *et al.*, 2016, Rajasree *et al.*, 2012)~~[16-17]. The physical stability of formulations was evaluated by using physical parameters including ~~such as~~ physical appearance, color, odor and homogeneity. All physical parameters were inspected through visual inspection.

Measurement of pH

The p~~P~~H value of the prepared formulations was measured by using digital p~~P~~H meter. The solution of gel and ointment were dissolved in 100 ml of distilled water and stored for 2 hr. The p~~P~~H measurement~~ed~~ in each formulation was done in triplicate and the average value was calculated.

Viscosity

Viscosity of gel and ointment formulations was~~ere~~ measured using Brookfield viscometer with spindle. Using spindle number LV-64 at 100 rpm and temperature was maintained at 25±2°C.

Chemical stability test

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Chemical stability test used to detect scopoletin (standard reagent) of the formulations was carried out for 36 days by measuring at initial day and 36 days after. At various temperature conditions including room temperature (25±2°C), cold (4°C) and heating-cooling cycle (kept in hot oven at 45 °C for ~~about~~ 48 hours and kept in cold temperature at 4°C for ~~about~~ 48 hours). The chemical stability of formulations was evaluated by using High-performance liquid chromatography (HPLC) ~~(Nithya *et al.*, 2003)~~[18].

HPLC Procedure

A Schimadzu LC-10 was used with UV detector set at 283 nm having Eclipes XDB-C18 column (4.6 mm × 150 mm; 5µm I.D.). ~~Twenty was adjusted at 35°C ± 1°C.~~ The mobile phase was a mixture of 0.1% phospholic acid~~r~~ and acetonitrile (82:18) with a flow rate of 1.0 ml/ min.

~~Twenty µl of~~ The ~~each~~ sample solution (20 microliter at 35±1°C) was injected and chromatogram was recoded. Peak area for each sample was measured and comparison was made between reference and sample solution~~s~~ peaks.

RESULTS

The objective of the current study is comparative studies on physicochemical properties of *Morinda citrifolia* gel and ointment formulations.

Extraction of plant material

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The simple method was used for the preparation of the extract. The percentage yield of methanolic extract of *Morinda citrifolia* was found to be 8.8%.

Determination of phytochemical screening

Phytochemical screening studies of *Morinda citrifolia* revealed the presence of anthraquinone, cardiac glycosides, coumarins, tannins, alkaloids, phenols and flavonoids which corresponds to previous research and shows that the extracted method of this researcher is reliable. Results obtained were summarized in Table 3.

Table 3: Evaluation of phytochemical screening

No. Plant constituents	Results
Anthraquinone	+
Cardiac glycosides	+
Saponin	-
Coumarins	+
Tannins	+
Phenols and flavonoids	+
Alkaloids	+

Note; + = present, - = Absent

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Evaluation of topical gel and ointment

Physical evaluation

All physical parameters were inspected through visual inspection. Results showed that gel formulation was found only to be changed in color (other physical parameters did not change). But ointment formulation was found to have a change in color in all of the conditions with a homogeneity change in heating-cooling cycle condition only. Results are shown in Table 5-6.

Measurement of pH

PH of the gel and ointment were measured by using digital PH meter. The gel and ointment formulations average value were about 5.77±0.15 and 5.68±0.14, respectively. Results are given in Table 5-6.

Viscosity

The viscosities of gel and ointment formulations were determined by using Brookfield viscometer. Measuring with all temperature conditions after 36 days, viscosities in the gel formulation did not change, but it was increased in the ointment formulation at heating-cooling cycle condition only. The viscosities of the formulations were reported in Table 5-6.

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Table 5: Physical evaluation of gel formulation

Physical evaluation	Initial	36 Days after		
		25±2°C	4°C	Heating -cooling cycle
Gel formulation				
Physical appearance	Clear	Clear	Clear	Clear
Color	Light Brown	Dark brown	Brown	Brown
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Homogeneity	Good	Good	Good	Good
pH	5.42±0.09	5.87±0.14	5.91±0.15	5.89±0.21
Viscosity	11980.96±16.50	11830.56±19.43	12550.80±25.60	14150.30±21.30

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Table 6: Physical evaluation of ointment formulation

Physical evaluation	Initial	36 Days after		
		25±2°C	4°C	Heating -cooling cycle
Ointment formulation				
Physical appearance	Semi-solid	Semi-solid	Semi-solid	Semi-solid
Color	Light Brown	Dark brown	Brown	Dark brown
Odor	Characteristic	Characteristic	Characteristic	Characteristic
Homogeneity	Good	Good	Good	Separate layer
pH	5.56±0.11	5.62±0.12	5.73±0.14	5.81±0.20
Viscosity	58980.21±75.68	59240.96±68.50	81940.72±85.27	Error

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Chemical evaluation

The chemical stability of the formulations was evaluated by detecting and compared the amount of scopoletin at various times and temperature conditions. Results show that on the initial day, scopoletin in gel formulation was found to be 3 folds higher than in ointment formulation. On day 36, scopoletin in gel formulation decreased without significant compared to the initial day at both room and cold temperature while it had significant decrease in heating-cooling cycle condition. Scopoletin in the ointment formulation had a significant decrease in all tested conditions. Results are shown in Fig. 1, Fig. 2 and Fig. 3 and Table 4.

Table 4: Chemical evaluation of gel and ointment formulation

Formulations	Scopoletin (mg/100g sample)			
	Initial	36 Days after		
		25±2°C	4°C	Heating -cooling cycle
Gel formulation	16.38±0.56	15.46±0.19	15.81±0.09	12.87±0.22*
Ointment formulation	4.89±0.34*	2.58±0.06†	3.55±0.06†	0.90±0.02†

* $p<0.05$ when compared to gel formulation on the initial day

† $p<0.05$ when compared to ointment formulation the initial day

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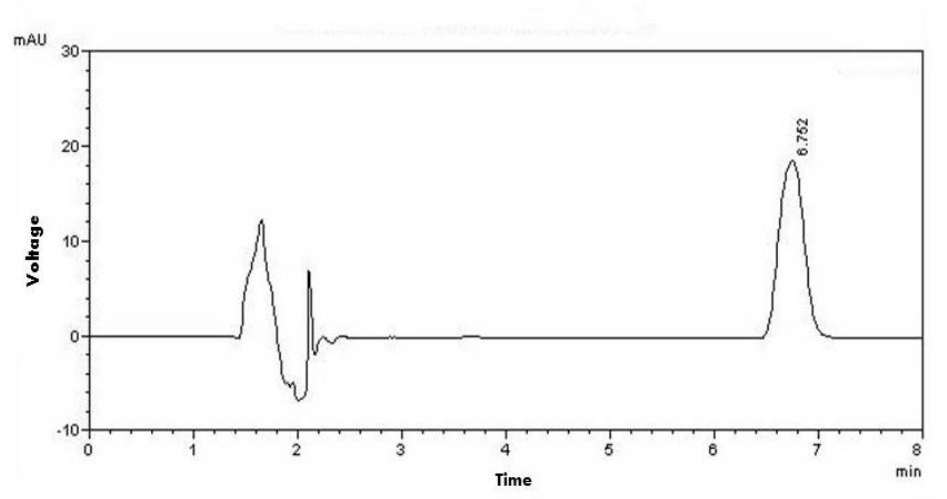

Fig. 1: Chromatogram on the initial day of scopoletin (reference)

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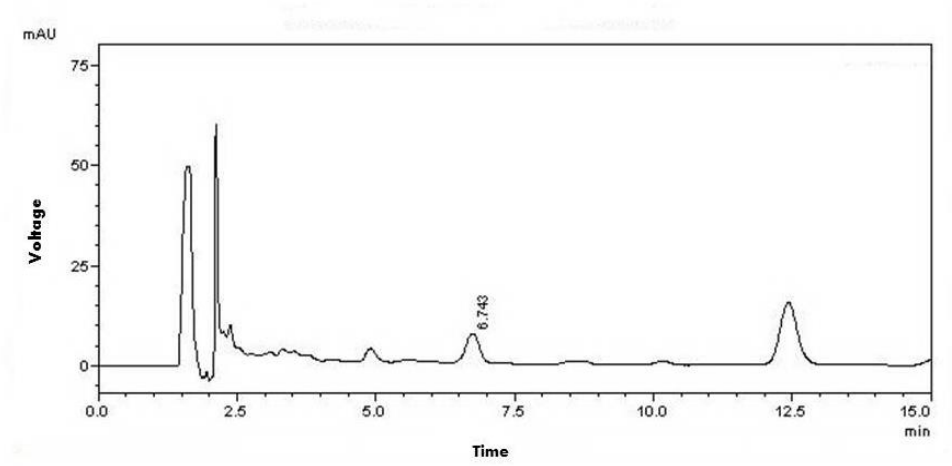

Fig. 2: Chromatogram on the initial day of gel formulation

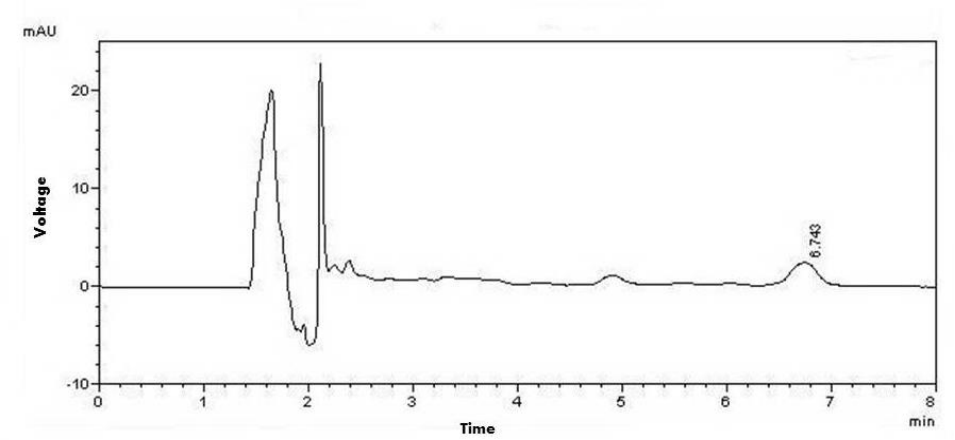

Fig. 3: Chromatogram on the initial day of ointment formulation

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DISCUSSION

Morinda citrifolia is a widely used herb and commonly found in Southeast Asian countries. It has been used in medicine for a long time. It has various medicinal properties such as helping to eliminate toxins in the body, stimulate the immune system, antioxidants, anti-inflammatory antibacterial, antiviral anti-tubercular, antitumor, anthelmintic, analgesic, hypotensive and wound healing effects. In *vivo* study, it supports the wound healing effect due to the found active substances in *Morinda citrifolia* extracts, namely proxeronine, scopoletin, anthraquinone, vitamins, amino acids [19]. Those active substances play a role in reducing inflammation and wound healing [20]. This study found that *Morinda citrifolia* extract contains actives substances such as anthraquinone, cardiac glycosides, coumarins, tannins, alkaloids, phenols and flavonoids which corresponds to previous research and shows that the extracted method of this researcher is reliable.

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At the present, products from noni extract has various forms but topical form, gel or ointment, detailed information regarding its wound healing capability are not completely documented. Thus, these studies were first reported to comparative studies on physicochemical properties of noni formulation in various conditions.

Development and evaluation of *Morinda citrifolia* extracts in gel and ointment formulations containg 10% extract. Physical stability test of the formulations were carried out for 36 days by measuring in the initial (0 day) and second time (36 days after) at various temperature conditions. The physical stability of formulations was evaluated by using physical parameters such as physical appearance, color, odor and homogeneity. All physical parameters were inspected through visual inspection. Results showed that gel formulation was found physical parameters did not change only color to be changed. But ointment formulation was found to have a change in color in all of the conditions with a homogeneity change in heating-cooling cycle condition only which change in color of gel and ointment formulation maybe caused by the oxidizing reaction. Chemical stability gets evaluated by detecting scopoletin on the initial day at various temperature conditions. The scopoletin was found to be 3 folds more in gel formulation than in ointment formulation. And after 36 days only at heating-cooling cycle condition found scopoletin significant decrease but ointment formulation found scopoletin significant decrease in all conditions. The ointment formulation found scopoletin less than gel formulation maybe the formulation was a separated layer and physical appearance very hard due to the formulation not dissolve well when measured by using of the HPLC, its found scopoletin less. In addition, ointment formulation has properties of drug release lower than gel formulation [21]. Therefore,

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the detection of scopoletin found less which according to the experimental results. At heating-cooling cycle condition is not appropriate store of this gel and ointment formulations.

AND DISCUSSION

Morinda citrifolia is a widely used herb and commonly found in Southeast Asian countries. It has been used in medicine for a long time. It has various medicinal properties such as helping to eliminate toxins in the body, stimulate the immune system, antioxidants, anti-inflammatory antibacterial, antiviral anti tubercular, antitumor, anthelmintic, analgesic, hypotensive and wound healing effects. In vVivo study, it supports the wound healing effect due to the found active substances in *Morinda citrifolia* extracts, namely proxeronine, scopoletin, anthraquinone, vitamins, amino acids etc (Manimaran *et al*., 2007, Sumitra, 2014, Vijayapandi *et al*., 2014). Those active substances play a role in reducing inflammation and wound healing (Afa *et al*., 2010). The simple method was used for the preparation of the extract. The percentage yield of methanolic extract of *Morinda citrifolia* was found to be 8.8%. Phytochemical screening studies of *Morinda citrifolia* revealed the presence of anthraquinone, cardiac glycosides, coumarins, tannins, alkaloids, phenols and flavonoids which corresponds to previous research and shows that the extracted method of this researcher is reliable. Results obtained were summarized in Table 3.

Development and evaluation of *Morinda citrifolia* extracts in gel and ointment formulations containingg 10% of the extract. Physical stability test of the formulations were carried out for 36 days by measuring in the initial (0 day) and second time (36 days after). At various temperature conditions including such as1) room temperature (25± 2°C), 2) cold (4°C) and 3) heating cooling cycle (kept in hot oven at 45 °C for about 48 hours and kept in cold temperatureat 4°C for about 48 hours) (Avinash *et al*., 2016, Rajasree *et al*., 2012). The physical

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stability of formulations was evaluated by using physical parameters includingsuch as physical appearance, color, odor and homogeneity. All physical parameters were inspected through visual inspection. Results showed that gel formulation was found only to be changed in color (other physical parameters did not change). But ointment formulation was found to have a change in color in all of the conditions with a homogeneity change in heating cooling cycle condition only which change in color of gel and ointment formulation maybe caused by the oxidizing reaction. Results are showngiven in Table 4 5.

The chemical stability of the formulations was evaluated Chemical stability gets evaluated by detecting and compared the amount of scopoletin at various times and temperature conditions. By measuring it on the initial day at room temperature, cold and heating cooling cycle, Results show that on the initial day, scopoletin in gel formulation was found to be 3 folds higher more in Gel formulation than in ointment formulation. On day 36, scopoletin in gel formulation decreased without significant compared to the initial day at both room and cold temperature while it had significant decrease in heating cooling cycle condition. And after 36 days at room and cold temperatures, scopoletin had insignificant decrease in the gel formulation. While in heating cooling cycle condition, scopoletin had a significant decrease. Scopoletin in the ointment formulation had a significant decrease in all tested conditions. of the ointment formulation when measured 36 days after, Rthe results are showngiven in Figures 1, 2 and 3 and Table 6.

Results from this study indicated that gel formulation of the methanolic fruit extract of *Molinda citrifolia* was more stable than ointment formulation. These may be due to the nature of compositions of ointment formulation. The appearance of ointment formation was separated layer and slightly hard compared to gel formulation. It may be limitation of the solubility of the

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~~extract in the ointment formulation. The ointment formulation found scopoletin less than gel formulation maybe the formulation was a separated layer and physical appearance very hard due to the formulation not dissolve well when measured by using of the HPLC, its found scopoletin less. In addition, ointment formulation has properties of drug release lower than gel formulation (Conners et al, 1986). Therefore, the detection of scopoletin found less in ointment formulation which according to the experimental results.~~

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CONCLUSION

Development and evaluation of *Morinda citrifolia* extract in gel and ointment formulations; based on the results of all experiments, it can be said that gel formulation is suitable for development due to its physical and chemical stability results which were better than ointment formulation results.

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Thus, gel formulation could become a media to be used for its medicinal properties. Results found in this research can be used as the base for further development of the gel formulation in order to obtain a formulation that can be used in drugs or in the form of topical treatment for wound healing or anti-inflammation effect.

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1. DECLARATION OF CONFLICTS OF INTEREST

2. AUTHORS CONTRIBUTION.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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Figure legends

Figure 1. Chromatogram on the initial day of scopoletin (reference)

Figure 2. Chromatogram on the initial day of gel formulation

Figure 3. Chromatogram on the initial day of ointment formulation

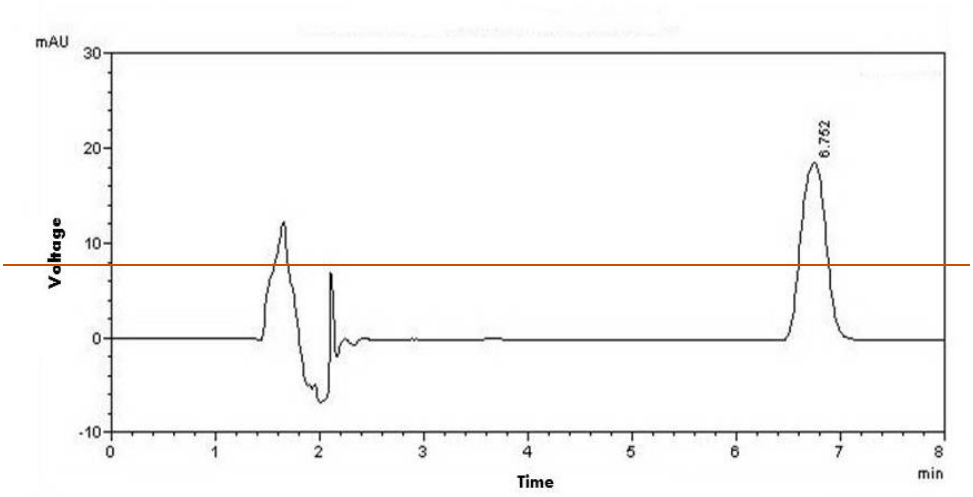

Figure 1. Chromatogram on the initial day of scopoletin (reference)

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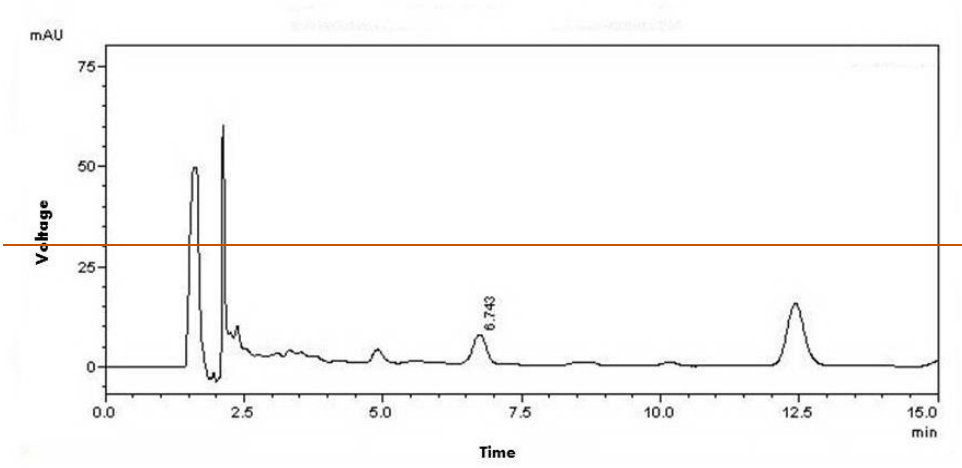
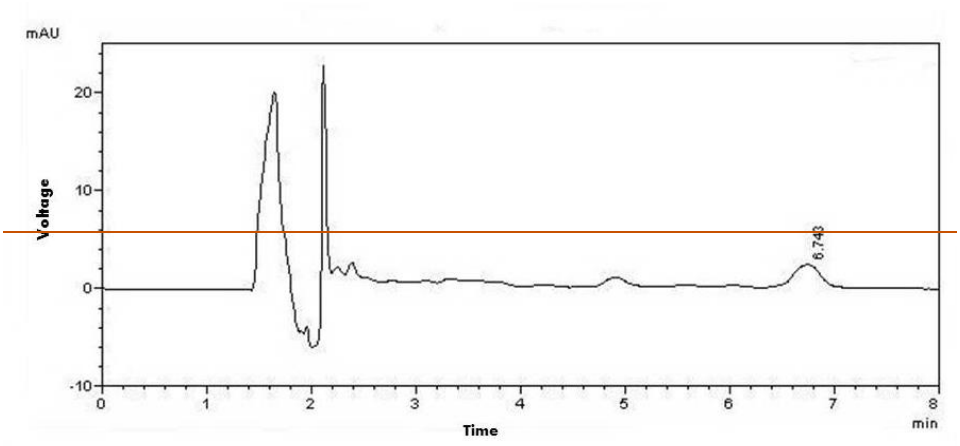


~~Figure 2. Chromatogram on the initial day of gel formulation~~



~~Figure 3. Chromatogram on the initial day of ointment formulation~~

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