

Lampiran c2. Bukti korespondensi dengan editor Karil JIB No 2 pada usulan pertama

No	Permasalahan	Komentar Tim PAK DIKTI	Klarifikasi
2	<p>Karil no 2</p> <p>Judul Artikel: Skin Penetration of Ubiquinone (Co-Q10) In Nanoemulsi on Delivery System Using Virgin Cocunut Oil (Vco)</p> <p>(Penulis ke 1 dari 3 penulis) dan sebagai Corresponding Author</p> <p>International Journal of Drug Delivery Technology; Vol. 8, Issues. 2; April-Juni 2018; Hal: 77-79 ISSN: 0975 4415 doi: 10.25258/ijddt.v8i2.13871 Impact Factor: 1.529 SJR 2018: 0.21; Q3; Coverage: 2011-ongoing H index: 7 Similarity Index (Turnitin): 5%</p>	<p>Tidak ada masalah. Dapat diterima sebagai syarat khusus</p>	<p>Tambahan Kronologi dan bukti korespondensi dengan editor jurnal terlampir</p>

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No	Tanggal	Keterangan
1	3 November 2017 (email 1: editor)	Pengiriman artikel melalui web jurnal; <i>Manuscript Submission Successful</i>
2	21 April 2018 (email 2: editor)	Naskah dengan ID 120602017DDTC <i>accepted after minor modifications</i>
3	21 April 2018 (email 3: author)	Pengiriman artikel yang sudah direvisi melalui web jurnal ada bukti artikel yang telah direvisi
4	23 April 2018 (email 4: author)	Pengiriman bukti biaya publikasi
5	23 April 2018 (email 5: editor)	Konfirmasi dari editor artikel akan segera di publish
6	04 Juli 2018 (email 6: editor)	Pengiriman galley proof oleh editor
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7. Keywords (2-10)

Nanoemulsion, Skin Penetration, Ubiquinone (co-Q10), Virgin Coconut Oil (VCO).

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List of correction:

No	Name Of Paragraph	Line	Uncorrected text	Correction
1	Abstract	13 dan and
2	RESULTS AND DISCUSSION	6 QE (8.5 cPas) QE (14.2 cPas)

SKIN PENETRATION OF UBIQUINONE (Co-Q10) IN NANOEMULSION DELIVERY SYSTEM USING VIRGIN COCONUT OIL (VCO)

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ABSTRACT

Ubiquinone (co-Q10) is a topical anti-aging with low solubility in water, so its penetration into the skin is also low. To increase its penetration ubiquinone (co-Q10) was loaded in the nanoemulsion delivery system using virgin coconut oil (VCO) as oil phase. Ubiquinone (co-Q10) in nanoemulsion formula consists of; ubiquinone (co-Q10), Tween 80, Span 80, ethanol 96%, VCO and acetate buffer solution pH 4.2 ± 0.5 with concentration; 1%; 18.66%; 1.92%; 3.42%; up to 100%, respectively. The characteristics of ubiquinone (co-Q10) nanoemulsion were observed in terms of droplet morphology by transmission electron microscope (TEM) and droplet size by particle analyzer, the pH and viscosity value. The ubiquinone (co-Q10) penetration test in the nanoemulsion system was compared with the emulsion on the rat skin. Result of this research showed the droplet morphology of ubiquinone (co-Q10) in nanoemulsion was spherical. The droplet size was 93.2 ± 2.78 nm. The pH value was 4.12 ± 0.02 , and the viscosity was 8.5 cPas. Penetrasi of ubiquinone (co-Q10) in nanoemulsion was deeper (269 ± 48.12 and 993 ± 36.49 μm) than in emulsion (26.33 ± 6.43 and 110.33 ± 9.124 μm), after 2 and 6 hours sample application.

Key words: Nanoemulsion, Skin Penetration, Ubiquinone (co-Q10), Virgin Coconut Oil (VCO).

INTRODUCTION

Nanoemulsion was known as a system to increase the solubility, and penetration of lipophylic substance^{1,2}. In this study nanoemulsion delivery system was used as vehicle of ubiquinone (co-Q10) wich is known as anti-aging. Ubiquinone (co-Q10) can prevent collagen and elastine damage and help to avoid wrinkle of the skin³. Nanoemulsion is an emulsion of oil in water (O/W) or water in oil (W/O) with the droplet size between 50 - 500 nm. Smaller

droplet size results in larger surface area it can increase the penetration of active ingredients⁴. For O/W nanoemulsion virgin coconut oil (VCO) used as oil phase in nanoemulsion because it can produced smallest droplet size than corn oil and soybean oil⁵.

MATERIALS AND METHODS

Research Material

Ubiquinone (Kangcare), virgin coconut oil (VCO), Tween 80 (Sigma Aldrich), Span 80 (Sigma Aldrich), ethanol 96% (E.Merck), acetic acid p.a (E.Merck), sodium acetate (E.Merck) p.a.

Research Instrument

Stirrer plate (Dragon Lab MS-Pro), ultrasonic (Branson 3510), Thermo shaker (Wine shake), pH meter (Eutech Instruments pH 700), Viscometer cone and plate, Transmission Electron Microscope (TEM) JEOL JEM 1400, Delsa™ Nano Submicron Particle Size and Zeta Potential Dynamic Light Scattering, Microscope Flourecents and Brightfield Olympus FSX100.

Experimental Animals

Animals used were male Wistar rats with the inclusion criteria: 8-10 weeks of age, 100-250 grams of weight, healthy condition, with no defect or injury.

Ubiquinone (co-Q10) Nanoemulsion and Emulsion Preparation

The nanoemulsion formula in this study refers to the modified formula from Erawati et al, 2014⁴. In this experiment the concentration of ubiquinone (co-Q10), Tween 80, Span 80, ethanol 96%, VCO and acetate buffer solution pH 4.2 ± 0.5 were: 1%; 18.66%; 1.92%; 3.42%; up to 100%, respectively.

The emulsion formula consists of; 1% ubiquinone (co-Q10) was dissolved in 35% VCO and then added with 22% of surfactant mixture (Tween 80 and Span 80), it was stirred until the mixture became homogeneous. Subsequently, a solution of acetate buffer pH 4.2 ± 0.5 up to 100%.

RESULTS AND DISCUSSION

The characteristics of ubiquinone (co-Q10) nanoemulsion (QN) and ubiquinone (co-Q10) emulsion (QE) included pH, droplets size and viscosity were presented in Table 1. Ubiquinone (Co-Q10) nanoemulsion and ubiquinone (co-Q10) emulsion both have same pH value were 4.12 ± 0.02 .

The droplets size of QN (93.2 ± 2.78 nm) was smaller than QE (10.55 ± 0.60 μ m). The viscosity of QN (8.5 cPas) lower than QE (14.2 cPas). The morphology of QN droplet by Transmission Electron Microscope JEOL JEM 1400 was presented in figure 1.

Histological preparation of skin penetration of ubiquinone (co-Q10) in emulsion at 2 hours (A1), at 6 hours (A2) after sample application and in nanoemulsion at 2 hours (B1), at 6 hours (B2) after sample application was determined by Microscope Olympus FX-100 42x zoom, presented in Figure 2. The result of in vivo skin penetration tests at two different times (2 and 6 hours after sample application) was known that panetration depth of ubiquinone (co-Q10) in nanoemulsion were 269 ± 48.12 and 993 ± 36.49 μ m, respectively. And than in emulsion were 26.33 ± 6.43 and 110.33 ± 9.124 μ m, respectively. It shows that penetration of ubiquinone (co-Q10) in noemulsion delivery system into the rat skin faster and deeper then in emulsion.

Ubiquinone (co-Q10) penetration rate in nanoemulsion is faster than in the emulsion caused by three factors; the first is the lower nanoemulsion viscosity than the emulsion, the second is the nanoemulsion droplets size smaller than the emulsion, so the movement of the active ingredient is easier in nanoemulsion. The third is the nenoemulsion system which increases the release rate so that it's much more active ingredients are ready to be penetrated into the skin^{6,7}.

CONCLUSION

Penetrasi of ubiquinone (co-Q10) in nanoemulsion was deeper (269 ± 48.12 dan 993 ± 36.49 μ m) than in emulsion (26.33 ± 6.43 and 110.33 ± 9.124 μ m), after 2 and 6 hours sample application on Wistar rats skin.

ACKNOWLEDGEMENT

The research was funded by Faculty of Pharmacy Airlangga University

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TABLE AND FIGURE

Table 1. Characteristics of ubiquinone (co-Q10) nanoemulsion (QN) and emulsion (QE)

Characteristic	QN	QE
pH	4.12 ± 0.02	4.12 ± 0.02
Droplet size	93.2 ± 2.78 nm	10.55 ± 0.60 μm
Viscosity	8.5 cPas	14.2 cPas

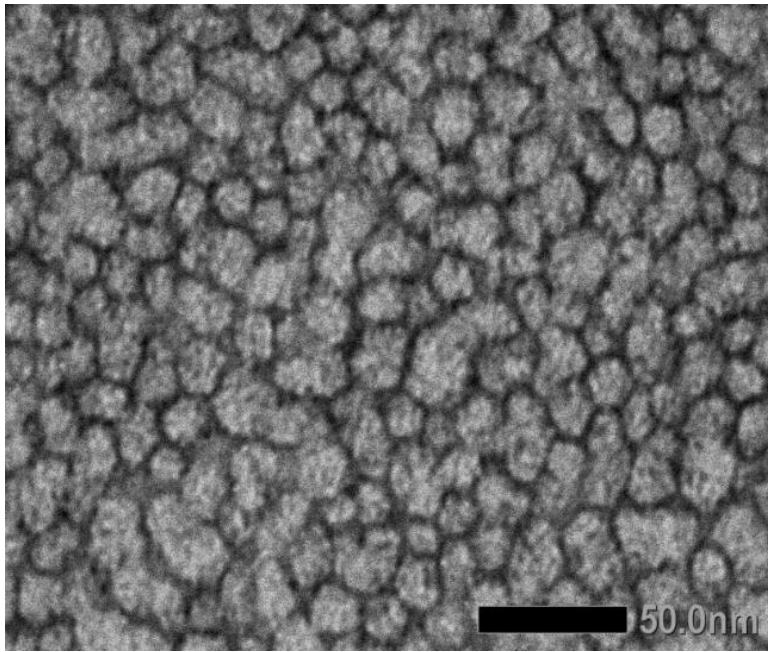


Figure 1. Droplet morphology of QN by Transmission Electron Microscope JEOL JEM 1400.

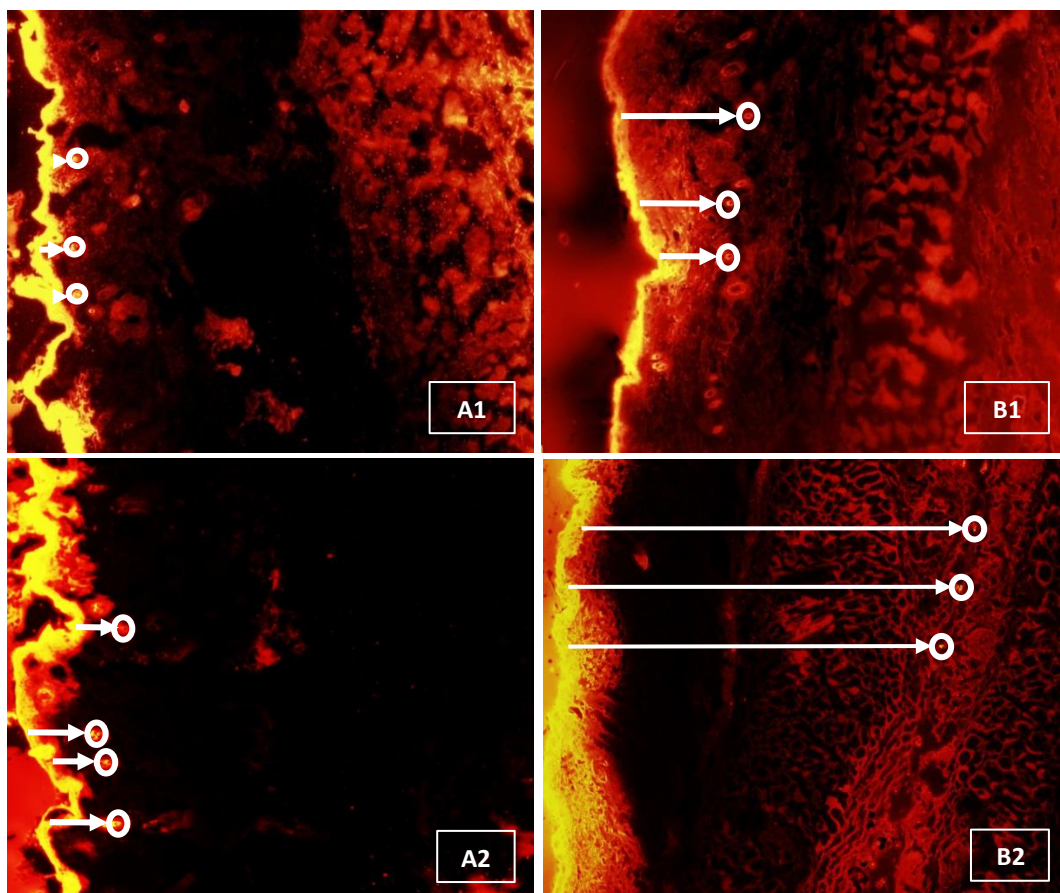


Figure 2: Histological preparation of skin penetration of co-Q10 in emulsion at 2 hours (A1), at 6 hours (A2) after sample application and in nanoemulsion at 2 hours (B1), at 6 hours (B2) after sample application was determined by Microscope Olympus FX-100 42x zoom.

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Re: SKIN PENETRATION OF UBIQUINONE (Co-Q10) IN NANOEMULSION DELIVERY SYSTEM USING VIRGIN COCONUT OIL (VCO)

Dari: IJDDT Journal (ijddtjournal@gmail.com)

Kepada: era_ffua@yahoo.co.id

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Ubiquinone (co-Q10) is a topical anti-aging with low solubility in water, so its penetration into the skin is also low. To increase its penetration ubiquinone (co-Q10) was loaded in the nanoemulsion delivery system using virgin coconut oil (VCO) as oil phase. Ubiquinone (co-Q10) in nanoemulsion formula consists of; ubiquinone (co-Q10), Tween 80, Span 80, ethanol 96%, VCO and acetate buffer solution pH 4.2 ± 0.5 with concentration; 1%; 18.66%; 1.92%; 3.42%; up to 100%, respectively. The characteristics of ubiquinone (co-Q10) nanoemulsion were observed in terms of droplet morphology by transmission electron microscope (TEM) and droplet size by particle analyzer, the pH and viscosity value. The ubiquinone (co-Q10) penetration test in the nanoemulsion system was compared with the emulsion on the rat skin.

Result of this research showed the droplet morphology of ubiquinone (co-Q10) in nanoemulsion was spherical. The droplet size was 93.2 ± 2.78 nm. The pH value was 4.12 ± 0.02 , and the viscosity was 8.5 cPas. Penetrasi of ubiquinone (co-Q10) in nanoemulsion was deeper (269 ± 48.12 dan 993 ± 36.49 μm) than in emulsion (26.33 ± 6.43 and 110.33 ± 9.124 μm), after 2 and 6 hours sample application.

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Nanoemulsion, Skin Penetration, Ubiquinone (co-Q10), Virgin Coconut Oil (VCO).

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Dari: tristiana erawati (era_ffua@yahoo.co.id)

Kepada: ijddtjournal@gmail.com

Tanggal: Kamis, 5 Juli 2018 03.40 GMT+7

Dear Editor
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I apologize to my manuscript there are still 2 typing errors on page 77 I gave highlight;

NO	Correction
1	<p>Section : ABSTRACT</p> <p>Page No : 77</p> <p>Line No : 10</p> <p>Column : 1</p> <p>Uncorrected Text: dan</p> <p>Correction : and</p>
2	<p>Section : RESULT AND DISCUSSION</p> <p>Page No : 77</p> <p>Line No : 8</p> <p>Column : 2</p> <p>Uncorrected Text: 8.5 cPas</p> <p>Correction : 14.2 cPas</p>

Please correct them.
Thank you

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Skin Penetration of Ubiquinone (Co-Q10) In Nanoemulsion Delivery System Using Virgin Coconut Oil (Vco)

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Received: 7th Dec, 17; Revised and Accepted: 21st Apr, 18; Available Online: 25th Jun, 2018

ABSTRACT

Ubiquinone (co-Q10) is a topical anti-aging with low solubility in water, so its penetration into the skin is also low. To increase its penetration ubiquinone (co-Q10) was loaded in the nanoemulsion delivery system using virgin coconut oil (VCO) as oil phase. Ubiquinone (co-Q10) in nanoemulsion formula consists of; ubiquinone (co-Q10), Tween 80, Span 80, ethanol 96%, VCO and acetate buffer solution pH 4.2 ± 0.5 with concentration; 1%; 18.66%; 1.92%; 3.42%; up to 100%, respectively. The characteristics of ubiquinone (co-Q10) nanoemulsion were observed in terms of droplet morphology by transmission electron microscope (TEM) and droplet size by particle analyzer, the pH and viscosity value. The ubiquinone (co-Q10) penetration test in the nanoemulsion system was compared with the emulsion on the rat skin.

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Keywords: Nanoemulsion, Skin Penetration, Ubiquinone (co-Q10), Virgin Coconut Oil (VCO).

INTRODUCTION

Nanoemulsion was known as a system to increase the solubility, and penetration of lipophilic substance^{1,2}. In this study nanoemulsion delivery system was used as vehicle of ubiquinone (co-Q10) which is known as anti-aging. Ubiquinone (co-Q10) can prevent collagen and elastin damage and help to avoid wrinkle of the skin³. Nanoemulsion is an emulsion of oil in water (O/W) or water in oil (W/O) with the droplet size between 50 - 500 nm. Smaller droplet size results in larger surface area it can increase the penetration of active ingredients⁴. For O/W nanoemulsion virgin coconut oil (VCO) used as oil phase in nanoemulsion because it can produce smallest droplet size than corn oil and soybean oil⁵.

MATERIALS AND METHODS

Research Material

Ubiquinone (Kangcare), virgin coconut oil (VCO), Tween 80 (Sigma Aldrich), Span 80 (Sigma Aldrich), ethanol 96% (E.Merck), acetic acid p.a (E.Merck), sodium acetate (E.Merck) p.a.

Research Instrument

Stirrer plate (Dragon Lab MS-Pro), ultrasonic (Branson 3510), Thermo shaker (Wine shake), pH meter (Eutech Instruments pH 700), Viscometer cone and plate, Transmission Electron Microscope (TEM) JEOL JEM 1400, Delsa™ Nano Submicron Particle Size and Zeta Potential Dynamic Light Scattering, Microscope Fluorescents and Brightfield Olympus FSX100.

Experimental Animals

Animals used were male Wistar rats with the inclusion criteria: 8-10 weeks of age, 100-250 grams of weight, healthy condition, with no defect or injury.

Ubiquinone (co-Q10) Nanoemulsion and Emulsion Preparation

The nanoemulsion formula in this study refers to the modified formula from Erawati et al, 2014⁴. In this experiment the concentration of ubiquinone (co-Q10), Tween 80, Span 80, ethanol 96%, VCO and acetate buffer solution pH 4.2 ± 0.5 were: 1%; 18.66%; 1.92%; 3.42%; up to 100%, respectively.

The emulsion formula consists of; 1% ubiquinone (co-Q10) was dissolved in 35% VCO and then added with 22% of surfactant mixture (Tween 80 and Span 80), it was stirred until the mixture became homogeneous. Subsequently, a solution of acetate buffer pH 4.2 ± 0.5 up to 100%.

RESULTS AND DISCUSSION

The characteristics of ubiquinone (co-Q10) nanoemulsion (QN) and ubiquinone (co-Q10) emulsion (QE) included pH, droplets size and viscosity were presented in Table 1. Ubiquinone (Co-Q10) nanoemulsion and ubiquinone (co-Q10) emulsion both have same pH value were 4.12 ± 0.02 . The droplets size of QN (93.2 ± 2.78 nm) was smaller than QE (10.55 ± 0.60 μm). The viscosity of QN (8.5 cPas) lower than QE (14.2 cPas). The morphology of QN droplet

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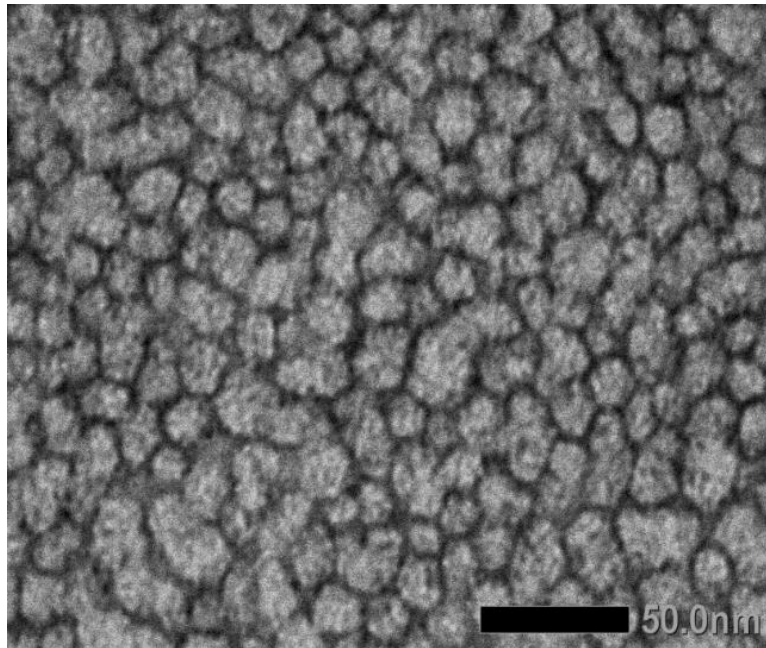


Figure 1: Droplet morphology of QN by Transmission Electron Microscope JEOL JEM 1400.

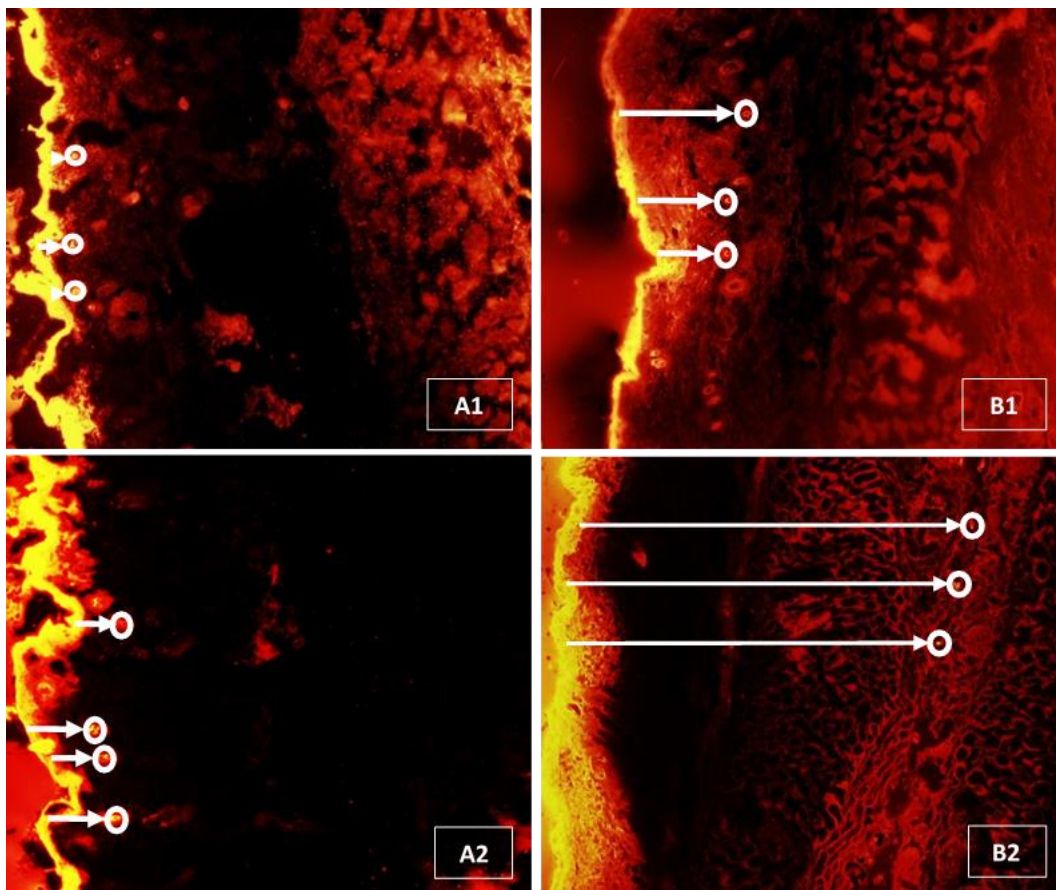


Figure 2: Histological preparation of skin penetration of co-Q10 in emulsion at 2 hours (A1), at 6 hours (A2) after sample application and in nanoemulsion at 2 hours (B1), at 6 hours (B2) after sample application was determined by Microscope Olympus FX-100 42x zoom.

by Transmission Electron Microscope JEOL JEM 1400 was presented in figure 1. Histological preparation of skin penetration of ubiquinone (co-Q10) in emulsion at 2 hours (A1), at 6 hours (A2) after

sample application and in nanoemulsion at 2 hours (B1), at 6 hours (B2) after sample application was determined by Microscope Olympus FX-100 42x zoom, presented in Figure 2. The result of in vivo skin penetration tests at two

Table 1: Characteristics of ubiquinone (co-Q10) nanoemulsion (QN) and emulsion (QE).

Characteristic	QN	QE
pH	4.12 ± 0.02	4.12 ± 0.02
Droplet size	93.2 ± 2.78 nm	10.55 ± 0.60 µm
Viscosity	8.5 cPas	14.2 cPas

different times (2 and 6 hours after sample application) was known that penetration depth of ubiquinone (co-Q10) in nanoemulsion were 269 ± 48.12 and 993 ± 36.49 µm, respectively. And than in emulsion were 26.33 ± 6.43 and 110.33 ± 9.124 µm, respectively. It shows that penetration of ubiquinone (co-Q10) in noemulsion delivery system into the rat skin faster and deeper then in emulsion.

Ubiquinone (co-Q10) penetration rate in nanoemulsion is faster than in the emulsion caused by three factors; the first is the lower nanoemulsion viscosity than the emulsion, the second is the nanoemulsion droplets size smaller than the emulsion, so the movement of the active ingredient is easier in nanoemulsion. The third is the nenoemulsion system which increases the release rate so that it's much more active ingredients are ready to be penetrated into the skin^{6,7}.

CONCLUSION

Penetrasi of ubiquinone (co-Q10) in nanoemulsion was deeper (269 ± 48.12 dan 993 ± 36.49 µm) than in emulsion (26.33 ± 6.43 and 110.33 ± 9.124 µm), after 2 and 6 hours sample application on Wistar rats skin.

ACKNOWLEDGEMENT

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