

ANTI-INFLAMMATORY ACTIVITY OF PARA METHOXY CINNAMIC ACID (PMCA) IN NANOEMULSION USING SOYBEAN OIL

by Widji Soeratri

Submission date: 14-Oct-2019 09:39AM (UTC+0800)

Submission ID: 1192104198

File name: METHOXY_CINNAMIC_ACID_PMCA_IN_NANOEMULSION_USING_SOYBEAN_OIL.pdf (1.51M)

Word count: 1904

Character count: 9654



ANTI-INFLAMMATORY ACTIVITY OF PARA METHOXV CINNAMIC ACID (PMCA) IN NANOEMULSION USING SOYBEAN OIL

Tristiana Erawati M., Pharmaceutics Department of Faculty of Pharmacy, Universitas Airlangga, Surabaya, era_fua@yahoo.co.id, Anneke Lodraswarj p., Pharmaceutics Department of Faculty of Pharmacy, Universitas Airlangga, Surabaya, Nanda Ghernasjh N.C., Pharmaceutics Department of Faculty of Pharmacy, Universitas Airlangga, Surabaya, Noorma Rosita, Pharmaceutics Department of Faculty of Pharmacy, Universitas Airlangga, Surabaya, Suwaldi Martodjhardjo, Pharmaceutics Department of Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Wjdh Soeratri, Pharmaceutics Department of Faculty of Pharmacy, Universitas Airlangga, Surabaya.

1 INTRODUCTION

Inflammation is a protective mechanism of the local microcirculation to tissue injuries caused by physical trauma, stimulation by hazardous chemicals, heat, antigen-antibody reaction and the effect of microbial.[2] It is known to be involved in the inflammatory reactions such as release of histamine, bradykinin, prostaglandins, fluid cell migration, extravasations, tissue break down and repair which are aimed at host defense and usually activated in most disease conditions. Para methoxy cinnamic acid (PMCA) known has topical anti-inflammatory effect but only 0.64 compare with Na-diclophenac.[4] Its cause PMCA is a poorly soluble drug substance (BCS II), the solubility in acetate buffer pH 4.2 ± 0.2 was 70.04 ± 0.66 mg/liter[3] So in this study to increase the solubility PMCA loaded nanoemulsion using soybean oil. And then the anti-inflammatory activity of PMCA in nanoemulsion was measured by the release rate, penetration rate through rat skin using Franz diffusion cell and histological test on mice's ear skin.

MATERIAL AND METHODS

Research Material:

Para methoxy cinnamic Acid (Sigma Aldrich), soybean oil (PT Kurniajaya), Tween 80 (Sigma Aldrich), Span 80 (Sigma Aldrich), ethanol 96 % (Merck), acetic acid (Merck), sodium acetate (Merck), NaCl (Merck), NaH2PO4 (Merck), Na2HPO4 (Merck), croton oil (Sigma) and aquademineralisata (PT Brataco)

Animals

Male Wistar rats (150 - 230 gm) and mince (20 - 30 gm) were taken from PUSVETMA Suraba-

2 ya. The animals were housed under standard conditions of temperature (25±2)°C, 12/12 hours light/dark cycles and fed with standard pellets. All animal experiments were conducted with the permission from Animal Care and Use Committee (ACUC) of Veterinary Faculty, Airlangga University, Indonesia. (Reference number; 378-KE).

Research Method

Nanoemulsion formula containing PMCA PMCA in nanoemulsion produced base on the formula presented in Table 1.

| Materials | Concentration(%) |
|--------------------------------------|------------------|
| PMCA | 0.2 |
| Soybean oil | 2.66 |
| Span 80 | 1.92 |
| Tween 80 | 18.66 |
| Ethanol 96% | 3.42 |
| Acetate buffer solution pH 4.2 ± 0.2 | ad 100 |

Table 1. PMCA Nanoemulsion Formula

Nanoemulsion formula used in this study is the result of a previous study by Erawati et.al, using a combination of surfactant Tween 80 and Span 80 with a ratio of 9:1 (having HLB 14), the ratio of surfactant and co surfactant 6:1, the ratio of oil phase (soybean oil) and water phase (acetate buffer solution pH 4.2 ± 0.2) is 27.5:1. [3]

Solubility test

PMCA solubility test; on the nanoemulsion





using soybean oil (as oil phase) added with 500 mg PMCA, then it was sonicated for 10 minutes and shaking with 150 rpm for 60 minutes. And then, the amount of PMCA dissolved in nanoemulsion was determined using spectrophotometer. After that the nanoemulsion PMCA characterized include; density, viscosity, pH, droplet morphology, droplet size and polydispersity index.

Release test

Membrane Preparation; the membrane used in the test release of PMCA in nanoemulsion system is a cellophane membrane. Membrane cut to size, then immersed in aqua-demineralization for ± 12 hours. A moment before use, the membrane is drained until no water is dripping, and then mounted on the surface of the receptor compartment of Franz diffusion cell.

Measurement the amount of the PMCA release from the nanoemulsion; receptor compartment of Franz diffusion cell filled with phosphate buffer pH 6.0 ± 0.2 up to full. Then, 2 ml of nanoemulsion PMCA inserted into the donor compartment. Experimental temperature is set and maintained at a temperature of $32 \pm 2^\circ\text{C}$. Magnetic stirrer rotated at a speed of 100 rpm. Samples of 1 ml were taken within a certain time interval, i.e. at 0, 5, 10, 15, 30, 45 minutes, and then 1, 1.5, 2, 3, 4, 6, 8, 10, 12, 24 hours. Immediately after sampling medium was replaced with phosphate buffer pH 6.0 ± 0.2 with a volume of samples taken. Subsequently, samples were taken observed with spectrophotometer. PMCA concentration in the sample was calculated using the regression equation of standard curve. Determination of PMCA cumulative amount released per unit membrane area (mg/cm^2) was calculated from the concentration obtained each time ($\mu\text{g}/\text{ml}$) which had been corrected with the Wurster's equation. Furthermore, multiplied by the number of medium and divided by the membrane surface area. The results obtained by the cumulative number of PMCA released per unit time. The release profile of PMCA, is

done by making a relations curve between the cumulative number of PMCA released (mg/cm^2) versus time (minutes). The release rate of (Flux release) PMCA was obtained from the slope of the regression equation in the steady state.

Penetration test

Membrane Preparation; skin male Wistar rats that had been shaved used as the membrane in the penetration test of PMCA in nanoemulsion system.

Measurement the amount of PMCA penetrate through rat skin; receptor compartment of Franz diffusion cell filled with phosphate buffer pH 7.0 ± 0.2 up to full. Then, 1 ml of nanoemulsion PMCA inserted into the donor compartment. Samples of 1 ml were taken within a certain time interval as in release test.

RESULT AND DISCUSSION

The PMCA solubility in nanoemulsion 3.07 ± 0.19 g/liter (presented in Table 2) increased than its solubility in acetate buffer pH 4.2 (pH 0.2 is 70.04 ± 0.66 mg/liter). The characteristics of nanoemulsion containing PMCA presented in Table 3; the density value was 1.0263 ± 0.0002 is almost equal to the density of water; the viscosity was $5.58 \pm 0.05\text{cP}$; the pH value was 4.47 ± 0.006 it was in the range of human skin pH, so it will not cause irritation; the droplet size was 57.3 ± 7.6 nm and the polydispersity index was 0.548 ± 0.044 it was indicate a moderate particle size distribution. (1) The droplet morphology of empty nanoemulsion and nanoemulsion containing PMCA in saturated solubility by TEM. type JEM-1400 was resented in Figure 1.

| Medium | The amount of PMCA dissolved |
|------------------------------------|------------------------------|
| Nanoemulsion | 3.07 ± 0.19 g/liter |
| Acetate buffer pH 4.2 \pm 0.2 | 70.04 ± 0.66 mg/liter |

Table 2. The solubility of PMCA in nanoemulsion and in acetate buffer pH 4.2 \pm 0.2



| The characteristics of nanoemulsion containing PMCA | |
|---|-----------------|
| density | 1.0263 ± 0.0002 |
| viscosity | 5.58 ± 0.05 cP |
| pH | 4.47 ± 0.006 |
| droplet size | 57.3 ± 7.6 nm |
| polydispersity index | 0.548 ± 0.044 |

Table 3. The characteristics of nanoemulsion containing PMCA

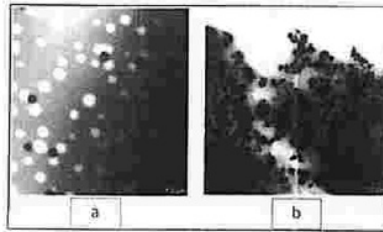


Figure 1. Droplet morphology of a) empty nanoemulsion and b) nanoemulsion containing PMCA in simulated solubility by TEM (JEM-1400)

The release profile and the release rate of PMCA in acetate buffer pH 4.2 and in nanoemulsion were presented in figure 2 and figure 3. After investigate for 24 hours (1440 minutes) the result shows that the release rate of PMCA in nanoemulsion ($0.4024 \pm 0.0339 \mu\text{g}/\text{cm}^2/\text{minute}$) increased compare with it in acetate buffer pH 4.2 is $0.0239 \pm 0.0003 \mu\text{g}/\text{cm}^2/\text{minute}$.

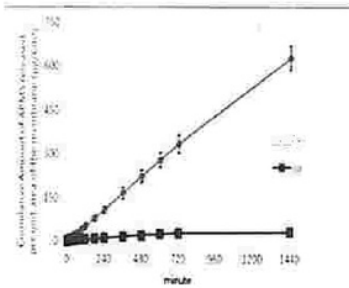


Figure 2. Release profile of PMCA in acetate buffer pH 4.2 ± 0.2 (control) and in nanoemulsion (FI*)

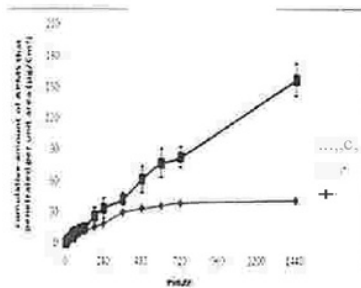


Figure 2. Penetration profile of PMCA in acetate buffer pH 4.2 ± 0.2 (control) and in nanoemulsion (FI*)

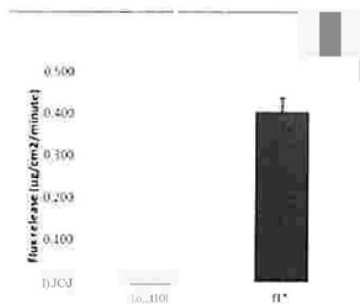


Figure 3. Histogram of release rate of PMCA in acetate buffer pH 4.2 ± 0.2 (control) and in nanoemulsion (FI*)

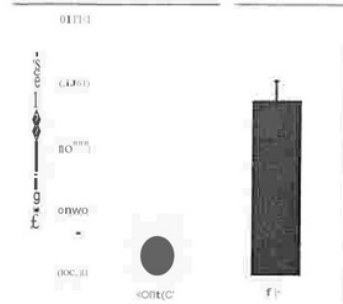


Figure 4. Histogram of penetration rate of PMCA in acetate buffer pH 4.2 ± 0.2 (control) and in nanoemulsion (FI*)





Also the penetration rate of PMCA in nanoemulsion was increased too (0.1513 \pm 0.0314 $\mu\text{g}/\text{cm}^2/\text{minute}$) compare with the penetration rate of PMCA in acetate buffer pH 4.2 (0.0341 \pm 0.0003 $\mu\text{g}/\text{cm}^2/\text{minute}$) as presented in figure 4 and 5. The increased of penetration rate of PMCA in nanoemulsion caused by 1) the solubility of PMCA in nanoemulsion increased (more than 43x compare with the solubility of PMCA in acetate buffer pH 4.2) and 2) the surfactant and co surfactant in nanoemulsion formula can function as enhancers.

From figure 6 and table 4, known that the anti-inflammatory effect of PMCA in nanoemulsion (FI*) higher than the anti-inflammatory effect of PMCA in acetate buffer pH 4.2 (control). The result of statistical test using ANOVA-one way ($P = 95\%$), known there are no significant different between the ears mice skin thickness after treated with PMCA in nanoemulsion (FI*) with health skin (K-) but thinner than inflammation skin (K+) also with the ears mice skin after treated with PMCA in acetate buffer pH 4.2 (control).

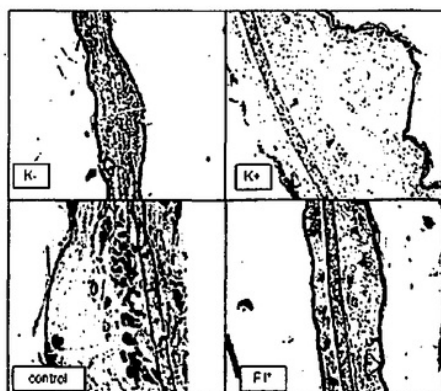


Figure 6. The histology profile of ears mice skin, health skin (K-), inflammation skin (K+), after treated with PMCA in acetic buffer pH 4.2 (control), and in nanoemulsion (FI*)

| Sample | The Average Of Skin Thickness (μm) |
|---------|--|
| K- | 282.96 \pm 36.80 |
| K+ | 592.53 \pm 59.81 |
| Kontrol | 541.69 \pm 56.56 |
| FI* | 310.56 \pm 30.76 |

Table 4. The average of ears mice skin after treated with PMCA in acetate buffer pH 4.2 (control), and in nanoemulsion (FI*) compare with health skin (K-) and inflammation skin (K+).

CONCLUSION

The nanoemulsion with soybean oil as drug delivery system can increase the anti-inflammatory activity of PMCA.

ACKNOWLEDGMENT

Thank to Indonesia Government (DIKTI) who give Research Fund through Rector of Universitas Airlangga (through LPPM-UA).

REFERENCES

1. Ouan C.Y., Xia Z.Y., Gui B.S., Xue J. F., Ouyang J.M, 2013, Changes in urinary nanocrystallites in calcium oxalate stone formers before and after potassium citrate intake. International Journal of Nanomedicine, Vol. 8, p. 909-918.
2. Mahesh G, Ramkanth S, Saleem MTS. Anti-Inflammatory drugs from medicinal plants A comprehensive review. International Journal of Review in Life Sciences 2011; 1(1): 1-10.



ICPP.f2014

Proceeding
The 1st International Conference
on Pharmaceutics & Pharmaceutical Sciences

3. Tristiana Erawati M, Esti Hendradi, Widji Soeratri, 2014, Praformulation Study Of p-Methoxycinnamic Acid (PMCA) Nanoemulsion Using Vegetable Oils (Soybean Oil, Corn Oil, VCO), IntJ Pharm Pharm Sci, ISSN-0975-1491, Vol. 6, Issue 2, 2014, 99-101
4. Widji Soeratri, Tristfana Erawatf M., Diny Rahmatika, Noorma Rosita, 2014, PMCA Dose as Topical Antiinflammation and Its Penetration Study Through Full-thick Rat Skin and Without Stratum Comeum, Indonesian Journal of Pharmacy and Pharmaceutical Science, ISSN- 2406-9388. Vol. 1, No. 1, June 2014 p. 28-30

ANTI-INFLAMMATORY ACTIVITY OF PARA METHOXY CINNAMIC ACID (PMCA) IN NANOEMULSION USING SOYBEAN OIL

ORIGINALITY REPORT

12%

SIMILARITY INDEX

11%

INTERNET SOURCES

4%

PUBLICATIONS

0%

STUDENT PAPERS

PRIMARY SOURCES

| | | |
|---|--|-----|
| 1 | www.ijppsjournal.com Internet Source | 10% |
| 2 | www.scitechnol.com Internet Source | 1% |
| 3 | Noha Ibrahim El-sherif, Rehab N. Shamma, Ghada Abdelbary. "In-situ gels and nail lacquers as potential delivery systems for treatment of onychomycosis. A comparative study", Journal of Drug Delivery Science and Technology, 2018 Publication | <1% |
| 4 | Goyal, A.. "Application of orthogonal collocation and regression techniques for recovering parameters of a two-pathway transdermal drug-delivery model", Computers and Chemical Engineering, 20070119 Publication | <1% |
| 5 | www.thieme-connect.de Internet Source | <1% |

Exclude quotes Off

Exclude matches Off

Exclude bibliography On

ANTI-INFLAMMATORY ACTIVITY OF PARA METHOXY CINNAMIC ACID (PMCA) IN NANOEMULSION USING SOYBEAN OIL

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5
