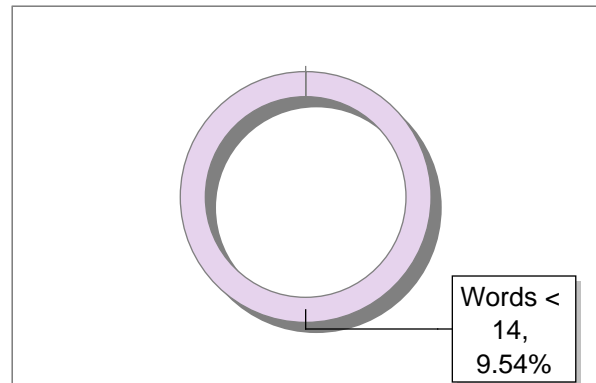
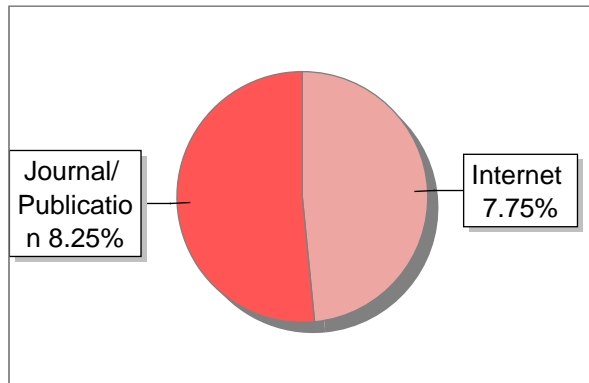
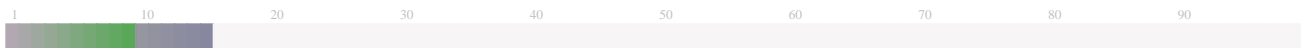


Submission Information

| | |
|---------------------|---|
| Author Name | MUHAMMAD FARIEZ KURNIAWAN |
| Title | Anti-inflammatory Activity Effect of Ficus carica |
| Paper/Submission ID | 1491142 |
| Submitted by | anjas.bakry@staff.uad.ac.id |
| Submission Date | 2024-03-04 13:48:13 |
| Total Pages | 8 |
| Document type | Article |

Result Information

Similarity **16 %**



Exclude Information

| | |
|-------------------------------|--------------|
| Quotes | Excluded |
| References/Bibliography | Excluded |
| Sources: Less than 14 Words % | Not Excluded |
| Excluded Source | 19 % |
| Excluded Phrases | Not Excluded |

Database Selection

| | |
|------------------------|---------|
| Language | English |
| Student Papers | Yes |
| Journals & publishers | Yes |
| Internet or Web | Yes |
| Institution Repository | Yes |

A Unique QR Code use to View/Download/Share Pdf File



DrillBit Similarity Report

16

SIMILARITY %

51

MATCHED SOURCES

B

GRADE

A-Satisfactory (0-10%)
B-Upgrade (11-40%)
C-Poor (41-60%)
D-Unacceptable (61-100%)

| LOCATION | MATCHED DOMAIN | % | SOURCE TYPE |
|----------|---|----|---------------|
| 2 | plosjournal.deepdyve.com | 1 | Internet Data |
| 3 | springeropen.com | 1 | Internet Data |
| 4 | docplayer.net | 1 | Internet Data |
| 5 | e-journal.unair.ac.id | 1 | Publication |
| 6 | academicjournals.org | 1 | Publication |
| 7 | springeropen.com | 1 | Internet Data |
| 8 | academicjournals.org | <1 | Publication |
| 9 | An alternative instrumental method for fabric pilling evaluation based on comput by Jasinska-2014 | <1 | Publication |
| 10 | coek.info | <1 | Internet Data |
| 11 | hindawi.com | <1 | Internet Data |
| 12 | www.joplink.net | <1 | Publication |
| 13 | A diterpenoid compound, excisanin A, inhibits the invasive behavior of by Qin-2013 | <1 | Publication |
| 14 | journal.unair.ac.id | <1 | Internet Data |

| | | | |
|----|---|----|---------------|
| 15 | worldwidescience.org | <1 | Internet Data |
| 16 | aij.batan.go.id | <1 | Publication |
| 17 | jurnal.ugm.ac.id | <1 | Publication |
| 18 | mmrjournal.biomedcentral.com | <1 | Publication |
| 19 | nature.com | <1 | Internet Data |
| 20 | Viability of probiotic strains <i>Lactobacillus acidophilus</i> NCFM and <i>Bifidobacteri</i> by Lalii-Petronijevi-2015 | <1 | Publication |
| 21 | redcol.minciencias.gov.co | <1 | Publication |
| 22 | 196.44.162.39 | <1 | Publication |
| 23 | Medicinal plants brought by Indian indentured immigrants A comparative review o by Mahomoodally-2019 | <1 | Publication |
| 24 | oamjms.eu | <1 | Publication |
| 25 | NiO NanocrystallineReduced Graphene Oxide Composite Film with Enhanced Electroc by Lang-2017 | <1 | Publication |
| 26 | documentop.com | <1 | Internet Data |
| 27 | doczz.es | <1 | Internet Data |
| 28 | ejournal.undip.ac.id | <1 | Internet Data |
| 29 | ejournal.undip.ac.id | <1 | Internet Data |
| 30 | eprints.uns.ac.id | <1 | Publication |
| 31 | etheses.uin-malang.ac.id | <1 | Publication |
| 32 | moam.info | <1 | Internet Data |

| | | | |
|----|---|----|---------------|
| 33 | New evidence for a critical role of elastin in calcification of native heart val by Id-2011 | <1 | Publication |
| 34 | smujo.id | <1 | Publication |
| 35 | www.dx.doi.org | <1 | Publication |
| 36 | llibrary.co | <1 | Internet Data |
| 37 | academicjournals.org | <1 | Publication |
| 38 | academicjournals.org | <1 | Publication |
| 39 | cjmb.org | <1 | Internet Data |
| 40 | journal.unair.ac.id | <1 | Internet Data |
| 41 | Measurement of breast skin viscoelasticity and a pilot study on the potential ra by Gorodetsky-1999 | <1 | Publication |
| 42 | moam.info | <1 | Internet Data |
| 43 | openscholar.dut.ac.za | <1 | Internet Data |
| 44 | recentscientific.com | <1 | Publication |
| 45 | spandidos-publications.com | <1 | Internet Data |
| 46 | Synthesis of Inorganic-Organic Oligomers Including Cyclotriphosphazenes and the by Kajiwara-1981 | <1 | Publication |
| 47 | uad.ac.id | <1 | Internet Data |
| 48 | www.ajpe.org | <1 | Internet Data |
| 49 | www.nature.com | <1 | Internet Data |
| 50 | academicjournals.org | <1 | Publication |

| | | | |
|-----------|--|----|-------------|
| 69 | Study on chemical constituents of different species of by Wan-2020 | <1 | Publication |
|-----------|--|----|-------------|

| | | | |
|-----------|--|----|-------------|
| 77 | www.dx.doi.org | <1 | Publication |
|-----------|--|----|-------------|

EXCLUDED SOURCES

| | | | |
|----------|--|----|-------------|
| 1 | www.ijper.org | 19 | Publication |
|----------|--|----|-------------|

MUHAMMAD FARIEZ KURNIAWAN 1* , MUH INDRA IRAWAN 1 , ARIFFADLI PRAKOSO 1 ,
NINING SUGIHARTINI 2 1School of Pharmacy, Faculty of Medicine and Health Sciences,

Universitas Muhammadiyah Yogyakarta, Indonesia 2Faculty of Pharmacy, Universitas Ahmad
Dahlan Yogyakarta, Indonesia *Corresponding Author : fariez@umy.ac.id Received: 09.11.19,

Revised: 15.12.19, Accepted: 13.01.20 Copyright©2018 by authors, all rights reserved. Authors
agree that this article remains permanently open access under the terms of the Creative

Commons Attribution License 4.0 International License ABSTRACT Figs leaves (Ficus carica
Linn.) and Sidr leaf (Ziziphus mauritania Linn.) are rich in phytochemical, one of them is flavonoid.

These two plants have been used as a traditional medicine to treat several ailments, such as
inflammation. On the other hand, the usage of fresh figs and sidr leaves is uncomfortable and the
efficacy of the effect is immeasurable. The aim of this study was to determine the presence of the

anti-inflammatory effect on the extract of the raw material and also to create an optimal cream
formulation for the extract. This study used 15 groups of male BALB/c mice strand which were

given treatment as follows: normal control, negative control, positive control, sidr extract 2,5%; sidr
extract 5%; figs extract 2,5%; figs extract 5%; combination extract 2,5%; combination extract 5%;
sidr cream 2,5%; sidr cream 5%; figs cream 2,5%; figs cream 5%; combination cream 2,5%;

combination cream 5%. The anti-inflammatory activity was evaluated by measuring the thickness
of epidermis in the skin tissue and descriptive observation of inflammatory cells and expression of

COX-2. Earlier, mice were given croton oil on the back to induce the inflammation. After 3 days
treatment of cream and extract, mice were sacrificed to obtain histopathological dosage made of

hematoxylin-eosin staining and immunohistochemistry COX-2. The result showed group control
sidr extract 2,5%; sidr extract 5%; figs extract 2,5%; figs extract 5%; combination extract 2,5%;

combination extract 5%; sidr cream 2,5%; sidr cream 5%; figs cream 2,5%; figs cream 5%;
combination cream 2,5%; combination cream 5% had the ability to reduce thickness of epidermis

significantly in statistic ($p < 0,05$) compared to negative group control. In other hand, compared to
positive group control there was no significant result and the positive control was better in reducing

inflammation than the control group. Keywords : figs leave extract, sidr leaves extract, cream, anti-
inflammatory INTRODUCTION Figs are included in the group of mulberry trees (Moraceae). Figs
leaf was traditionally used for hypercholesterolemia, hyperglycemia, and as a topical antibacterial.

There have been many studies that have led to figs. Phytochemical and entomological studies in
figs proved that the fruit and figs leaves contain many bioactive compounds such as phenolic

compounds, phytosterols, organic acids, anthocyanins, triterpenoids, coumarins, and volatile
compounds such as hydrocarbons, and aliphatic alcohols [11]. Figs are also referred to the Quran

as one of the letter titles, namely Surah At-Tiin. Other plants mentioned in Al Quran are leaves of
sidr, in QS. AS Saba verse 16. Sidr leaves are known for containing phytochemical active

elements with the highest number of saponins, followed by tannins, alkaloids, phenolic
compounds, and flavonoids [1]. Figs and sidr leaves are plants that are widely used in Traditional

Arab Medicine [3] because of the content they have. Leaves with pharmacological activity used as

antibacterial, antioxidant, antitumor, and anti-inflammatory [3] are also traditionally used as a therapy for diabetes, cancer, anemia and skin diseases [2]. Figs leaves according to Bouyahya et

al (2016) contain polyphenol and flavonoid compounds. Sidr leaves contain active compounds of polyphenols, flavonoids, alkaloids, terpenoids, and saponins [15]. They also contains fagarin, -sitosterol, stigmasterol, -amyrin, lupeol, betulin [7] and catechins and spinosin [8]. Sidr leaves and their Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 921| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 seed are potential for antioxidant [5] antitumor, anticancer [1], antibacterial [15], thrombolytic agents [7], and anti-inflammatory [8]. From the above research, it has also been proven that sidr leaves have anti-inflammatory effect, since one of the ingredients in sidr is flavonoids which are active substances that plays a role in the anti-inflammatory. Although there have been many studies on the effects of the two plants above, the studies that have been carried out have not been matched by further research in terms of extract formulations of the two ingredients above into one dosage forms, one of which is an anti-inflammatory effect formed in topical dosage forms. From the problems and potential of figs and sidr leaves, it is necessary to conduct a study where figs and sidr leaf are formed in a topical formulation to enhance the therapeutic effect.

MATERIALS AND METHODS Materials The material used in this study were analytical scales (Mettler Toledo), blenders, vessels or jars, glassware (Iwaki Pyrex), funnels, stirrers, motion diffusion test equipment, ointment sticky test equipment, ointment dispersion test equipment, digital stirring hotplates (Thermo Fisher Scientific Cimarec), rotary evaporator, water bath (Memmerth), porcelain saucer, volume pipette, pipette pro, filter paper, aluminum foil, pH meter (Seven Easy Mettler Toledo), Microscope (Olympus). Dry figs leaves (Ficus carica) and sidr leaves (Ziziphus mauritania) were obtained from distributors of Olive Therapy House, croton oil to induce inflammation in mice obtained from distributors, 70% ethanol (Brataco®) for maceration, reagents photochemical screening reagents, ingredients for formulating anti-inflammatory cream dosage form in the form of Vaseline (Brataco®), Propylene glycol (Brataco®), Stearyl alcohol (Brataco®), Lauryl sulfate (Brataco®), oleic acid (Brataco®), and aquadest. Reagents for in vivo evaluation and irritation test. The test animals used were Balb / C strain mice. Extract of simplified powder The extraction method that the researcher used was the maceration method. Maceration started with weighing 1 kg of the simplified powder of figs leaves (Ficus carica) and sidr leaves (Ziziphus mauritania), then putting them into a vessel and adding 70% ethanol 10L. Maceration was carried out on the third day. On the seventh day, it was filtered and macerated using a Buchner funnel, then heated using a rotary evaporator instrument at a speed of 90 rpm at 80°C. Evaporation aims to concentrate on a solution of non-volatile solutes and volatile solvents [13]. The final stage of making this concentrated extract was the result of a liquid extract from the rotary process heated with a water bath at 80°C so that the concentrated extract was obtained and the yield was calculated. Phytochemical screening Extract of figs and sidr obtained were then screened qualitatively to determine whether there were flavonoid, tannin, anthraquinone,

saponins, alkaloids, and polyphenols or not. This photochemical screening was carried out by a color test reacted with reagents [6]. Cream Formulation The cream was made by the melting some ingredients. Solid materials such as stearyl alcohol were melted first at 60°C. Oil phases such as vaseline album, Propylparaben, stearyl alcohol, natrium lauryl sulfate, and oleic acid were mixed into the warm mortar until became homogeneous. Water-soluble materials namely propylene glycol and nipagin, were mixed until became homogeneous. Then the two phases were mixed until

they are became homogeneous. Then extract was added which has been dissolved with a little alcohol then stirred until became homogeneous. The cream was put into a tightly closed container. The Cream formulas are shown in table 1. Physical Properties Test PH testing was carried out using a pH meter inserted into the cream, then the pH meter was seen with normal parameters from 4.5 to 6.5 [17]. Spreading test was carried out by weighing 0.5 grams of cream and placing it in the middle of the petri dish in the upside down position. Then another petri dish was put on top of the cream and left for 1 minute. It was continued by measuring it in a spread cream meter. 50 grams cream was added as additional load and left for 1 minute then measured in diameter after the load reached 500 grams [17]. Adhesive test was carried out by weighing 0.23 grams of cream before being placed on top of a glass object that has been determined in size. The cream was placed on the glass of the object. The cream was released with a weight of 80 grams, and it was noted that the two glass objects were released [17]. Viscosity measurements and determination of flow properties were carried out using a viscometer Rheosys Merlin spindle cone and plate 2.0/30mm®. The measurement of viscosity started by pressing start and taking place within a certain time, the viscosity of the cream and the cream flow curve were generated automatically[14]. Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 922| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 Table 1. The cream formula of ethanolic extract of fig and sidr leaves KT 2,5% : Cream with figs leaves extract 2,5% KT 5% : Cream with figs leaves extract 5% KB 2,5% : Cream with sidr leaves extract 2,5% KB 5% : Cream with sidr leaves extract 5% KK 2,5% : Cream with combination figs and sidr leaves extract 2,5% KK 5% : Cream with combination figs and sidr leaves extract 5% Evaluation of In Vivo Anti-inflammatory Cream Effect This research received approval from the UMY Committee of Ethics No. 371/EP-FKIK- UMY/VIII/2018. This study used ninety mice which were divided into fifteen treatment groups, each of which consisted of six mice of BALB / c strain. The nine groups included three control groups, namely one normal group, one positive control group with Voltaren® emulgel, and one group that was croton oil without healing. The other twelve groups were samples that were initially induced by inflammation with croton oil and received 2.5% figs extract cream, 5% figs extract cream, 2.5% sidr extract cream, 5% sidr extract cream, combination extract cream and sidr 2.5%, combination extract cream figs and sidr 5%, crude extract of 2.5% figs leaves, crude extract of 5% figs leaves, crude extract of sidr leaves 2.5%, crude extract of sidr leaves 5%, crude extract of combination figs leaves and sidr 2.5%, and crude extracts of combination of figs leaves and sidr leaves 5%. The group that received previous inflammatory induction was shaved on the back and aneared with

group that received previous inflammatory induction was shaved on the back and smeared with hair thresher (Veet®). After 24 hours, the back was dripped with 0.1 mL croton oil (0.1%). the first Inflammatory induction procedure was shaving the back of the mouse 2x2 cm wide. After 24 hours, the mouse was dropped with 0.1 ml of croton oil concentration of 0.1%. Thirty minutes later, an extract of 100 mg of cream was applied for three days with equal treatment. Then the mice were sacrificed. The skin collection area was the back with a treatment area of 1 x 1 cm. The skin tissue was then immersed in 10% formalin for the manufacture of histopathological dosage form by staining hematoxylin-eosin (HE) and COX-2 immunohistochemistry which was carried out according to standard methods in pathology laboratories, Faculty of medicine, UGM and Anatomical Pathology Laboratory, Hospital. Dr. Sardjito, Yogyakarta [18]. The results were

analyzed under a light microscope (Olympus) in the histology laboratory of the University of Muhammadiyah Yogyakarta. Analysis of COX-2 expression, inflammatory cells, and thick epidermis were done using Toupview® software. RESULTS AND ANALYSIS Phytochemicals screening Qualitative analysis was carried out on both samples to obtain an overview of the compounds contained in concentrated extracts of figs leaves and sidr. Examinations was carried out including TLC and the use of reagents that according to the content was thought to have the potential for efficacy. The results of the phytochemical test from the two samples are as follows. In this TLC test the stationary phase used was silica gel 60 f 254 and the mobile phase was ethyl acetate: methanol: water (70: 23,5: 30). based on the theory, Flavonoids will be detected with yellow spots if it was detected by UV light and caused color [9]. From this test the Rf value obtained was 0.8 for the three spots namely rutin (a) as standard, figs leaf extract (b), and sidr leaf extract (c). Due to yellow spots on Rf from both samples matched rutin Rf which was the standard for flavonoids, it was Material (g) Formula KB 2,5% KB 5% KT 2,5% KT 5% KK2,5% KK 5% Extract 2,5 5 2,5 5 2,5 5 Vaseline 10 10 10 10 10 10 Methylparaben 0,025 0,025 0,025 0,025 0,025 0,025 Propylparaben 0,015 0,015 0,015 0,015 0,015 0,015 Propylene glycol 8 8 8 8 8 8 Stearyl Alcohol 10 10 10 10 10 10 Lauryl sulfate 1 1 1 1 1 1 Oleic acid 4 4 4 4 4 4 Alcohol Qs. Qs. Qs. Qs. Aquadest ad 100 100 100 100 100 100 Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 923| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 concluded that figs and sidr leaves contain rutin as one of flavonoids type. In addition, there were also spots with an Rf value of 0.94 in the figs leaf samples whereas in sidr leaf there were spots with an Rf value of 0.91. This patch was thought to be another substance which was carried along in extraction, considering that figs leaf extract and sidr leaf were raw extracts. The results of TLC test are shown in figures 1. From the other phytochemicals screening, the extract of figs and sidr leaves contained alkaloids flavonoid, saponins, alkaloids, and polyphenols but no tannin and anthraquinone. Figures 1. The result of TLC test Physical Properties Test Viscosity is the ability of a dosage form to flow [12]. Viscosity is related to flow properties. Viscosity measurements can be done with various types of viscometer as needed; in this study, Rheosys Merlin II was used. From the result, we know that the kind of rheology was pseudoplastic. Viscosity is related to dispersion and adhesion

know that the kind of rheology was pseudoplastic. Viscosity is related to dispersion and adhesion of topical dosage form. Spread power itself has an inverse relationship with adhesion and viscosity, so the higher the viscosity of a sample, the greater the adhesion and the smaller the scattered power. The value of the spread of dosage form is usually inversely proportional to its viscosity. The higher the viscosity of the dosage form, the lower the spread value. Spread power tests were carried out to ensure even distribution of the cream when applied to the skin. In this study, a parallel plate method was used using round glass and millimeter blocks for scattering power measurements. According to Garg et al. (2002), proper dosage form have spreads of 5 to 7 cm. The actual measure of dispersion is subjective, and there are no specific standards. PH testing using a pH meter was inserted into the cream, then seen the pH meter with normal parameters 4.5 - 6.5 [17]. All of the cream formulations showed the value of pH between 5,01 – 5,28. Adhesive test is used to determine the maximum ability of cream dosage form to stick to the application area, namely the skin. An excellent cream adhesion, which can coat the surface thoroughly, does not clog pores and does not disturb the physiological functions of the skin [20].

Anti-inflammatory Test Results of Cream This study used six treatment groups, each of which consisted of 6 mice. Painting of hematoxylin-eosin (HE) and immunohistochemistry COX-2 were carried out according to the standard method in the Pathology laboratory of the Faculty of Medicine UGM and the Anatomical Pathology laboratory, RS. Dr. Sardjito, Yogyakarta [19]. Calculation of epidermal thickness was measured based on the average distance between the deepest epidermal layer and the outer measured from the three fields of view of each slice of skin tissue per test animal. The results of epidermal thickness are shown in figures 2. Figures 2. The microscopic image of the average epidermal width of skin tissue by staining hematoxylin-eosin (HE) 120x (a) normal enlargement, (b) negative control, (c) positive control, (d) extract group, and (e) cream formula group Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 924| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 Observation of inflammatory cells was carried out descriptively by comparing the field of view of each group where the field of view was taken from three perspectives. The presence of blackish brown spots can identify inflammatory cells. The observation of cells expressing COX-2 was carried out with 120x magnification in the field of view of the skin tissue slices of each group of test animals, based on the number of cells showing brown color in the cytoplasm or the core. Table 2. Results of measurement of epidermal thickness on 15 mice control groups Data from the anti-inflammatory power test table 2 the results of painting the HE dosage form showed that the thickness of the epidermis, in the normal control, was the least. This contrasts with the data in the negative control group that received treatment using a 100 µL induction compound of 4% croton oil. Croton oil is known to have irritant properties and can cause inflammation, so this oil is chosen as an inflammatory inductor [10]. Croton oil has the mechanism of activated phospholipase A2, which then secretes arachidonic acid from the cell membrane. This arachidonic acid is then metabolized to prostaglandin and leukotriene [16]. Based on statistical tests, there were significant differences in epidermal thickness between the normal

... statistical test, there were no significant differences in epidermal thickness between the normal control group and negative controls (inflammatory induction without administration of cream) ($p < 0.05$). The existence of significant differences in the induction method can be used to evaluate the anti-inflammatory activity of the cream formula made. Positive groups (topical anti-inflammatory products available on the market) function as a benchmark for the effectiveness of dosage form with products on the market. Microscopic images of positive controls showed lower epidermal thickness and were statistically significant when compared with negative controls. When compared with the normal group, the thickness of the epidermis showed slightly higher results, but not significantly different. With this, it can be concluded that market products are statistically significant effective in reducing thickening and even restoring skin thickness as normal. The treatment group in this study was divided based on several aspects, namely the aspect of the dose of the active substance, and the dosage form. There were two dosage variations, namely 2.5% and 5%, while the dosage form was divided into cream dosage form and raw extracts. The dosage variations were used to see the correlation of the amount of the active ingredient and the effectiveness of the therapy, while the dosage form compared the penetration power of the active substance in a cream dosage form with the active substance in the raw extract. By comparing each treatment group with the negative group, it can be proved that there was a difference in each group statistically ($\text{sig} < 0.05$), so it can be concluded that the treatment group had a significant

effect in reducing epidermal thickness. From the test results, it was found a number of treatments that were statistically not significant ($p > 0.05$), including sidr extract 2.5%; sidr extract 5%; figs extract 2.5%; sidr cream 2.5%; figs cream 2.5%; and 5% figs cream which can be concluded that statistically the treatment group has the ability to decrease epidermis which is relatively the same as the Group Epidermal thickness (μm) Normal control $407,07 \pm 23,65$ Negative control $678,90 \pm 110,61$ Positive control $408,57 \pm 33,82$ KT 2,5% $435,41 \pm 15,07$ KT 5% $427,68 \pm 28,44$ KB 2,5% $470,01 \pm 57,01$ KB 5% $450,87 \pm 28,19$ KK 2,5% $470,1 \pm 24,69$ KK 5% $472,58 \pm 19,10$ Figs leaves extract 2,5% $426,21 \pm 39,28$ Figs leaves extract 5% $454,55 \pm 40,01$ Sidr leaves extract 2,5% $429,15 \pm 14,63$ Sidr leaves extract 5% $446,09 \pm 16,04$ Combination extract of figs and sidr leaves 2,5% $463,38 \pm 55,31$ Combination extract of figs and sidr leaves 5% $458,60 \pm 19,64$ Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 925| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 market of Voltaren gel® products. Furthermore, there were several treatment groups that were statistically different, namely 5% figs extract; combination extract 2.5%; extract 5% combination; sidr cream 5%; combination cream 2.5%; 5% combination cream. In this study, a comparison was made between treatment groups to determine statistical effectiveness. The extract treatment group showed the same decrease in epidermal thickness activity ($p > 0.05$) except sidr leaf extract group 2.5% with combination group of sidr and figs leaf extract 5% ($p < 0.05$). Table 2 data shows the width of the epidermis of the combination extract group of 5% at $458.60 \mu\text{m}$, higher than the width of the epidermis of the sidr extract group 2.5% at $429.15 \mu\text{m}$. For the cream formulation group, it was found that 5% figs cream was cream with a mean epidermal thickness was $427.68 \pm$

28.44 μm . Statistically, a 5% figs cream has a significant difference compared to a 2.5% combination cream and a 5% combination cream, while the rest had no significant difference. The anti-inflammatory effect of ethanol extract of figs leaves and sidr leaves was supported by a decrease in the number of inflammatory cells and a reduction in the expression of cyclooxygenase 2 (COX-2) enzymes which were seen in observations under the microscope, and observation data are shown in figures 2 and 3 as follows: Figure 3. Microscopic description of COX-2 skin tissue expression with 300x (a) normal immunohistochemical staining, (b) negative control, (c) positive control, (d) extract group, and (e) group of cream formulas Figure 4. Microscopic picture of inflammatory cell tissue with staining of hematoxylin-eosin (HE) 120x (a) normal enlargement, (b) negative control, (c) positive control, (d) extract group, and (e) cream formula group Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of Ficus carica and Ziziphus mauritania leaves 926| International Journal of Pharmaceutical Research | Jan - March 2020 | Vol 12 | Issue 1 Based on Figure 2 it was known descriptively that COX-2 enzyme expression was identified from its descriptive shape such as a telephone receiver or showed a brown color on its core or cytoplasm [19]. Figure 3 illustrated descriptively that inflammatory cells were characterized by blackish patches [19]. In descriptive observations, there were more emergence of inflammatory cells and COX-2 expression in negative controls than in the normal group. These results indicated that croton oil can cause inflammation of the skin [10]. Inflammatory cells and COX-2 expression between treatment groups, both extracts and cream dosage form when compared with negative controls and normal groups were seen to have descriptive appearance differences, where the results of microscopic images of the formula group compared to negative controls showed fewer

numbers of inflammatory cells and COX-2, but when compared with normal controls it showed a higher number of inflammatory cells and COX-2 expressions. Microscopic observations comparing the cross-section of positive controls with the treatment group were also carried out to show the number of inflammatory cells and COX-2 expressions that emerged between the groups, where the results of the observation showed that the number of inflammatory cells and COX-2 was relatively equal. CONCLUSION The cream of ethanolic extract of figs leaves and leaves of sidr influences the descriptive observation subjectively to the microscopic image of COX-2 enzyme expression in skin tissue of mice induced by croton oil. The cream of ethanol extract of figs leaves and leaves of sidr has a descriptive effect on the microscopic image of inflammatory cells in skin tissue of mice induced by croton oil. The combination of ethanol extract of figs leaves and sidr leaves cannot be proven to have better efficacy in reducing epidermal thickness, a number of inflammatory cells and expression of COX-2 enzymes than single dosage form. REFERENCES 1. Abdallah, E.M., Elsharkawy, E.R., Eddra, A., 2016. Biological activities of methanolic leaf extract of Ziziphus mauritania. BIOSCIENCE BIOTECHNOLOGY RESEARCH COMMUNICATIONS 2016, 11. 2. Badgujar, S.B., Patel, V.V., Bandivdekar, A.H., Mahajan, R.T., 2014. Traditional Uses, Phytochemistry And Pharmacology Of Ficus Carica: A Review. Pharm. Biol. 52, 1487–1503. <https://doi.org/10.3109/13880209.2014.892515> 3. Bouyahya, A., Bensaid, M., Bakri, Y., Dakka,

N., 2016. Phytochemistry And Ethnopharmacology Of *Ficus Carica*. *Int. J. Biochem. Res. Rev.* 14, 1– 12. <https://doi.org/10.9734/ijbcrr/2016/29029> 4. Garg, A., Aggarwal, D., Garg, S. & Singla, A.K., 2002. Spreading of semisolid formulations: an update. *Pharmaceutical Technology*, 26(9), pp.84-105 5. Haeria, Hermawati, Tenri AUDP., 2016, Penentuan Kadar Flavanoid Total dan Aktivitas Antioksidan Ekstrak Daun Bidara (*Ziziphus spina- christi* L), *Journal Of Pharmaceutical and Medicinal Scienc.*, 1 (2), 57-61 6. Harborne, J.B., (1985). *Phytochemical methods—a guide to modern techniques of plant analysis*. 7. Hossain, M.J., Sikder, A.A., Kaiser, M.A., Haque, M.R., Chowdhury, A.A., Rashid, M.A., 2015. Phytochemical And Biological Investigations Of Methanol Extract Of Leaves Of *Ziziphus Mauritiana* Lam. 11 8. Kadioglu, O., Jacob, S., Bohnert, S., Naß, J., Saeed, M.E.M., Khalid, H., Merfort, I., Thines, E., Pommerening, T., Efferth, T., 2016. **Evaluating Ancient Egyptian Prescriptions Today: Anti- Inflammatory Activity Of *Ziziphus Spina-Christi***. *Phytomedicine* 23, 293–306. <https://doi.org/10.1016/J.Phymed.2016.01.004> 9. Koirewoa, Y.A., Fatimawali, dan W. I. Wiyono. 2012. Isolasi dan Identifikasi Senyawa Flavonoid dalm Daun Beluntas. Universitas Sam Ratulangi. Manado 10. Lan, M., Wan, P., Wang, Z.Y., Huang X.L., 2012, Analisis GC-MS Komponen Kimia dalam Minyak Biji Croton Tiglium, *Zhong Yao Cai journal*, 35(7) :1105-8. 11. Mawa, S., Husain, K., Jantan, I., 2013. *Ficus carica* L. (Moraceae): Phytochemistry, Traditional Uses, and Biological Activities. *Evidence-Based Complementary and Alternative Medicine* 2013, 1–8. <https://doi.org/10.1155/2013/974256> 12. Mitsui, T., (1993), *New Cosmetic Science*, Nanzado Ltd., Japan, pp. 14, 19-21 *Physiological Plant Pathology* 27, 255–256. [https://doi.org/10.1016/0048-4059\(85\)90073-6](https://doi.org/10.1016/0048-4059(85)90073-6) 13. Praptiningsih, Yulia. (1999). *Buku Ajar Teknologi Pengolahan*. FTP UNEJ: Jember 14. Putranti, W., Dewi, N.A., Widiyastuti, L., 2018. STANDARDIZATION OF EXTRACT AND CHARACTERIZATION OF EMULGEL FORMULA OF LENGKUAS (*Alpinia Galanga* (L.) Wild) RHIZOME EXTRACT. *Journal of Pharmaceutical Sciences and Community* 15, 81– 91. <https://doi.org/10.24071/jpsc.1521612> 15. Shad, A.A., Ahmad, S., Ullah, R., Abdel-Salam, N.M., Fouad, H., Rehman, N.U., Hussain, H., Saeed, W.,

2014. Phytochemical And Biological Muhammad Fariez Kurniawan et al / Anti-inflammatory Activity Effect of *Ficus carica* and *Ziziphus mauritania* leaves 927| *International Journal of Pharmaceutical Research* | Jan - March 2020 | Vol 12 | Issue 1 *Activities Of Four Wild Medicinal Plants*. *Sci. World J.* 2014, 1–7. <https://doi.org/10.1155/2014/857363> 16. Shah, B., Seth, A., dan Maheshwari, K., 2011, A Review on Medicinal Plants as a resource of Anti- inflammatory Agents, *Research Journal of Medicinal Plant*, 5(2): 101-115 17. Shovyana, H.H. dan Zulkarnain, A.K., 2013, Stabilitas Fisik dan Aktivitas Krim W/O Ekstrak Etanolik Buah Mahkota Dewa (*Phaleria macrocarpa* (scheff.) Boerl.) sebagai Tabis Surya, *Traditional Medicine Journal*, 18 (2), 109-117. 18. Sugihartini, N., 2013, Optimasi Komposisi Enhancer dan Emulgor pada Formulasi Krim Fraksi Etil Asetat Ekstrak Teh Hijau (*Camellia sinensis*, L) sebagai Sediaan Topikal Antiinflamasi, *Disertasi, Program Pascasarjana Fakultas Farmasi UGM, Yogyakarta*, 78-79 19. Sugihartini, N., Saridewi, R., M, U.R., Rahmawanti, F., Yuliani, S., Sophia, V., 2017. Anti- inflammatory Activity of *Camellia sinensis*, I. Extract Cream Combined with Vitamin C as Antioxidant on Croton Oil-induced

Inflamation in Male Mice Strain 20. BALB/C. Majalah Obat Tradisional 22, 73

<https://doi.org/10.22146/tradmedj.27915> 21. Voight, R., 1995, Buku Pelajaran Teknologi Farmasi, diterjemahkan oleh Soendari Noerono, 22. Gajah Mada University Press, Yogyakarta, 566- 567.

23. Lamia medouni-haroune, farid zaidi, sonia medouni-adrar, mouloud kecha (2018) olive pomace: from an olive mill waste to a resource,