

In Vivo Analgesic Activity of Omega-3 on Mice Induced Peripheral Pain

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Fish oil which contains omega 3 with the most types of Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) has the effect of pharmacology as anti-inflammatory, antioxidant and is good for heart disease where probably it can be used beneficially as an analgesic. Analgesics have several side effects including gastric ulcer, bleeding, even Steven Johnson's Syndrome, have been attributed to their use. This research aims to determine the analgesic effect of fish oil on male white mice induced to produced peripheral pain. We used acetic acid-induced male BALB/c white mice to investigate analgesic effect fish oil in vivo by Writhing method. From this research, fish oil decreased writhings number in mice dose 5, 10, 20 and 30 mg/kg compared to negative control ($P < 0.001$). The percentage inhibition of writhing at the dose 30 mg/kg is the highest among other dose (42.64%), while in the group positive control (acetylsalicylic acid 100 mg/kg) is 68.26%. We concluded that fish oil has analgesic effect which reduced writhings in male mice induced by acetic acid to produce peripheral pain.

Keywords: Fish oil, analgesic, omega-3, marine nutraceutical, pharmaceutical, antiinflammatory.

Analgesics are drugs that are often prescribed and effective as a therapy for pain and inflammation. Some diseases requiring analgesics therapy include osteoarthritis, rheumatoid arthritis, neuropathic pain, chronic headaches, and dysmenorrhea. However, analgesics have side effects, especially gastrointestinal disorders¹ that can interfere with the patient and the effect on decreasing blood flow to the kidneys if used for a long time.

Fish oil has the most omega-3 content with EPA and DHA types. Omega-3 is well known anti-inflammatory and has good effect on cardiovascular patients^{2,3}. EPA and DHA work to inhibit the enzyme cyclooxygenase, so it does not cause the

release of inflammatory mediators⁴. This compound is predicted to have safe and promising analgesic effects in patients with peripheral pain. They are natural products that are expected not to have side effects such as those given by NSAIDs. Thus, this study aims to determine the analgesic effect of fish oil on male white mice that are BALB/c strains induced to produce peripheral pain.

MATERIAL AND METHODS

Materials

Fish oil was obtained from a Golden Bear Laboratory. Acetic acid, a chemical induce peripheral pain was obtained from Merck, as

Table 1. Effect of fish oil on writhings

Group	Number of Writhings
Negative Control	104.6 ± 12.8
Positive Control	33.2 ± 6.8
Fish Oil 5 mg/kg	89.6 ± 3.6
Fish Oil 10 mg/kg	83.6 ± 4.2
Fish Oil 20 mg/kg	73.8 ± 3.8
Fish Oil 30 mg/kg	60.0 ± 3.8

well as the span and tween which are emulgators for acetylsalicylic acid. The male BALB/c mice weighing 20-30 gram were housed in the laboratory of Pharmacy Study Program at the Faculty of Medicine Hang Tuah University under standard conditions.

Methods

A total 30 male BALB/c mice were divided into six groups. Each group contained five rats. Group I was control (span and tween 5%), Group II received acetylsalicylic acid emulsion (100 mg/kg) given orally, Group III, IV, V, VI were given fish oil (5, 10, 20, 30 mg/kg). Analgesic activity were tested by Writhing Method. Every mice were induced pain by acetic acid 0.6% (intraperitoneal) about 30 minutes after administration of drug to be tested. Five minutes post administration of acetic acid writhing movements like elongation of body, abdominal constriction, trunk twisting, forelimb extension, hind limb extension and back arching (one of these) were counted cumulatively every 5 minutes for 60 minutes. The ethical clearance of this research was certified by KEP of Hang Tuah University with the number of 02/HC/DU/EC/KEPUHT/IX/2017.

The data obtained were analysed using SPSS version 22.0. The significance differences between groups was checked using ANOVA, followed by Duncan test.

RESULTS

The effect of fish oil on acetic acid induced writhing is presented in Table 1. Fish oil at the dose 5, 10, 20 and 30 mg/kg body weight produced highly significant ($P < 0.001$) reduction in the number of writhings in mice when compared to group I (span and tween 5%). The percentage inhibition of writhing at the dose 5, 10, 20 and 30

Table 2. Percentage inhibition of pain

Group	Percentage Inhibition of Pain (%)
Positive Control	68.26
Fish Oil 5mg/kg	14.34
Fish Oil 10 mg/kg	20.08
Fish Oil 20 mg/kg	29.44
Fish Oil 30 mg/kg	42.64

mg/kg are 14.34%, 20.08%, 29.44% and 42.64%, while in the group II (acetylsalicylic acid 100 mg/kg) is 68.26% as shown in Table 2.

DISCUSSION

Fish oil given at dose 5, 10, 20 and 30 mg/kg showed significant analgesic activity as compared to negative control (span and tween 5%). Nobre in 2013 reported that omega-3 from fish oil had antiinflammatory and nociceptive effect in mice⁵. Similarly Kunder *et al.*, in 2017 reported that DHA has promising analgesic activity in rats when combined with sodium valproate⁶.

The analgesic activity of fish oil contain omega-3 by decreasing pain threshold⁷. The mechanism of omega-3 lies in DHA which facilitates the release of β -endorphins so that release, aids GPR40 signaling, and induces antinociception receptors through μ - and opioid receptor stimulation^{8,9}. Another mechanism for reducing pain through suppression of an arachidonic acid cascade thus inhibiting proinflammatory production such as eicosanoids and cytokines^{10,11,12,13}.

In this study, the percentage inhibition of pain was 42,64%, while the percentage inhibition of pain from positive control was 68,26%. Limitations in this study were not carried out analgesic testing of fish oil at doses higher than 30 mg/kg to see if the higher the dose of fish oil could provide a higher analgesic effect. Further research is recommended to look at the combined effects of using fish oil with analgesics on pain and inflammatory diseases in pre-clinic and clinic settings.

CONCLUSION

Fish oil contained EPA and DHA has

shown promising analgesic activity and was almost comparable to acetylsalicyl acid. Fish oil has a potential to be analgesic, so it is necessary to conduct further research related to doses that can provide analgesic effects resembling standard therapy.

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