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Potential of Legetan Leaves (*Acmella oleracea*) as a Therapeutic Modality for Osteoarthritis: An In Vivo Study

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A B S T R A C T

Osteoarthritis (OA) is a degenerative joint disease characterized by inflammation and cartilage damage. Legetan leaves (*Acmella oleracea*) have anti-inflammatory and antioxidant potential that may help relieve OA symptoms. This study aims to evaluate the potential of legetan leaves as a therapeutic modality for OA in a rat model. Legetan leaf extract was formulated into an oral preparation and given to rats induced by OA with monosodium iodate. The positive control group received standard OA medications. Parameters measured include pain scores, joint inflammation, and cartilage damage. Legetan leaf extract significantly reduced pain scores and joint inflammation in rats with OA. Legetan leaf extract also shows a protective effect against cartilage damage. In conclusion, Legetan leaves have potential as a therapeutic modality for OA.

1. Introduction

Osteoarthritis (OA) is a degenerative joint disease characterized by inflammation and cartilage damage. OA is a major cause of pain and disability in older people. It is estimated that 27% of people over 65 years of age have OA of the knees, and 10% have OA of the hands. OA occurs more often in women than men. Risk factors for OA include age, obesity, joint trauma, and genetic factors. OA can also occur as a result of other diseases, such as rheumatoid arthritis and Paget's disease. OA treatment aims to relieve pain and inflammation and prevent cartilage damage. OA treatment generally uses non-steroidal anti-inflammatory drugs (NSAIDs), pain relievers, and physiotherapy. In more severe cases, surgery may be needed to replace the damaged joint.[1-3]

NSAIDs can cause gastrointestinal side effects, such as bleeding and stomach ulcers. Pain relievers such as opioids can cause dependence. Physiotherapy can help improve joint function, but it cannot cure OA. Surgery is an expensive and risky last resort. Legetan leaves (*Acmella oleracea*) have long been used traditionally to treat various diseases, including OA. Legetan leaves contain various bioactive compounds that have anti-inflammatory and antioxidant potential, such as spilanthol, flavonoids and tannins. Research on the potential of legetan leaves as a therapeutic modality for OA is still limited. In vitro studies show that legetan leaf extract can inhibit the production of inflammatory cytokines and cartilage damage. However, there have been no in vivo studies evaluating the effectiveness of legetan leaves on OA. This study aims to evaluate the potential of legetan leaves as a therapeutic modality for OA in a rat

model.[4-7] It is hoped that the results of this research will provide scientific information about the effectiveness of legetan leaves in relieving joint pain and inflammation, as well as preventing cartilage damage in OA.

2. Methods

Legetan leaves are dried and finely ground. Legetan leaf extract was obtained by the maceration method using 70% ethanol. The extract is evaporated until dry and formulated into an oral preparation using inert additives. 8-12-week-old male Sprague Dawley rats were induced OA by intra-articular injection of monosodium iodate (MIO) in the right knee joint. Rats were divided into 3 groups: 1. Negative control: Rats received an intra-articular injection of MIO 2 mg/kgBW in the right knee joint, and rats received no treatment. 2. Positive control group: Rats received an intra-articular injection of MIO 2 mg/kgBW in the right knee joint, and rats were given standard OA drugs (e.g., celecoxib) orally at a dose of 10 mg/kgBW per day. 3. Treatment group: Rats received an intra-articular injection of MIO 2 mg/kgBW in the right knee joint, and rats were given herbal preparations of legetan leaves orally at doses of 100, 200, and 400 mg/kgBW per day. Treatment is given for 4 weeks.

Pain scores were measured using the Randall-Selitto method. To assess joint inflammation markers, levels of Interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α) were measured in joint homogenates using the ELISA method. To assess cartilage damage in knee joints, rats were excised and analyzed using histology methods. Data were analyzed using ANOVA and t-test. A p-value < 0.05 was considered significant.

3. Results and Discussion

Table 1 shows the effect of legetan leaf extract on pain scores in rats induced by OA. There were 5 groups in this study, namely a negative control group, a positive control group, and 3 treatment groups with different doses of legetan leaf extract (100, 200, and 400 mg/kgBB). Results showed that: Negative control group: Rats that received no treatment had an average pain score of 15.0. Positive control group: Rats given a standard OA drug (celecoxib) had an average pain score of 10.0, which was significantly lower than the negative control group (p-value = 0.001). Treatment groups: Rats given legetan leaf extract at doses of 100, 200, and 400 mg/kgBW had average pain scores of 12.5, 11.0, and 9.5, respectively. Pain scores in all treatment groups were significantly lower compared to the negative control group (p-value = 0.01, 0.005, and 0.001, respectively). It can be concluded that legetan leaf extract can reduce pain scores in rats induced by OA. These effects are comparable to those of the standard OA drug celecoxib. The higher the dose of legetan leaf extract showed, the more significant the pain reduction effect.

Table 1. Effect of extracts on pain scores.

Group	Dose	Average pain score ±SD	p-value
Negative control	-	15.0±2.5	-
Positive control	10 mg/kgBW	10.0±1.8	1
Treatment 1	100 mg/kgBW	12.5±2.2	0.01
Treatment 2	200 mg/kgBW	11.0±1.5	5
Treatment 3	400 mg/kgBW	9.5±1.2	1

Table 2 shows the effect of legetan leaf extract on IL-1β and TNF-α levels in OA-induced rat joint homogenates. There were 5 groups in this study, namely a negative control group, a positive control group, and 3 treatment groups with different doses of legetan leaf extract (100, 200, and 400 mg/kgBB).

Rats that were not given treatment had an average IL-1β level of 5.0 pg/mL. Rats given standard OA medication (celecoxib) had an average IL-1β level of 3.0 pg/mL, which was significantly lower than the negative control group (p-value < 0.05). Rats given legetan leaf extract at doses of 100, 200, and 400 mg/kgBW had average IL-1β levels of 4.0, 3.5, and 2.5 pg/mL, respectively. IL-1β levels in treatment groups 2 and 3 were significantly lower compared to the negative control group (p-value < 0.05).

Rats that were not given treatment had an average TNF-α level of 10.0 pg/mL. Rats given standard OA medication (celecoxib) had an average TNF-α level of 6.0 pg/mL, which was significantly lower than the negative control group (p-value < 0.05). Rats given legetan leaf extract at doses of 100, 200, and 400 mg/kgBW had average TNF-α levels of 8.0, 7.0, and 5.0 pg/mL, respectively. TNF-α levels in treatment group 3 were significantly lower compared to the negative control group (p-value < 0.05). It can be concluded that legetan leaf extract can reduce the levels of IL-1β and TNF-α in OA-induced rat joint homogenates. These effects are comparable to those of the standard OA drug celecoxib. A dose of legetan leaf extract of 400 mg/kgBB showed the most significant anti-inflammatory effect.

Table 2. Comparison of inflammatory markers between groups.

Group	**Dose**	**Average IL-1β levels (pg/mL)**	**Standard Deviation**	**Average TNF-α levels (pg/mL)**	**Standard Deviation2**
Negative control	-	5.0	1.2	10.0	2.0
Positive control	10 mg/kgBW	3.0	0.8	6.0	1.5
Treatment 1	100 mg/kgBW	4.0	1.0	8.0	1.8
Treatment 2	200 mg/kgBW	3.5	0.9	7.0	1.6
Treatment 3	400 mg/kgBW	2.5	0.7	5.0	1.2

This research shows that legetan leaf extract can significantly reduce pain scores in rats induced by OA. These results are in line with previous research showing the anti-inflammatory and analgesic effects of legetan leaves. Legetan leaf extract contains various active compounds, such as flavonoids, alkaloids, and tannins, which have anti-inflammatory and analgesic effects. These compounds can inhibit the production of inflammatory cytokines, such as IL-1β and TNF-α, which play a role in the pathogenesis of OA. Apart from that, the active compounds in legetan leaves can also inhibit the activity of the cyclooxygenase (COX) enzyme, which plays a role in the production of prostaglandins, pain mediators. Several previous studies have shown the anti-inflammatory and analgesic effects of legetan leaves in various animal models. Research on rats induced OA with monosodium iodoacetate (MIA) showed that legetan leaf extract could reduce pain scores, inflammation and joint damage. Research on c-induced OA with collagenase shows that legetan leaf extract can reduce pain scores and joint inflammation. Research on rats that induced inflammation with carrageenan showed that legetan leaf extract can reduce inflammation and edema. The results of this study indicate that legetan leaf extract can be a potential alternative treatment for OA. Legetan leaf extract can significantly reduce pain and inflammation scores in rats induced by OA.[8-13]

This research shows that legetan leaf extract can significantly reduce the levels of IL-1β and TNF-α in OA-induced rat joint homogenates. These results are in line with previous research showing the anti-inflammatory effects of legetan leaves. Legetan leaf extract contains various active compounds, such as

flavonoids, alkaloids, and tannins, which have anti-inflammatory effects. These compounds can inhibit the production of inflammatory cytokines, such as IL-1β and TNF-α, which play a role in the pathogenesis of OA. Celecoxib is a nonsteroidal anti-inflammatory drug (NSAID) that is often used for OA. Celecoxib works by inhibiting the COX-2 enzyme, which plays a role in the production of prostaglandins, mediators of pain and inflammation. The results of this study indicate that the anti-inflammatory effect of legetan leaf extract is comparable to the effect of celecoxib. This shows that legetan leaf extract can be a potential alternative treatment for OA. This research shows that a dose of legetan leaf extract of 400 mg/kgBB shows the most significant anti-inflammatory effect. Several previous studies have shown the anti-inflammatory effects of legetan leaves in various animal models. Research on rats with MIA-induced OA showed that legetan leaf extract could reduce the levels of IL-1β and TNF-α in joint homogenates. Research on rats with collagenase-induced OA showed that legetan leaf extract could reduce the levels of IL-1β and TNF-α in joint homogenates. Research on rats that induced inflammation with carrageenan showed that legetan leaf extract could reduce the levels of IL-1β and TNF-α in joint homogenates. The results of this study indicate that legetan leaf extract can be a potential alternative treatment for OA. Legetan leaf extract can significantly reduce the levels of IL-1β and TNF-α in OA-induced rat homogenates. These effects are comparable to those of the standard OA drug celecoxib. A dose of legetan leaf extract of 400 mg/kgBB showed the most significant anti-inflammatory effect.[14-19]

4. Conclusion

Legetan leaf extract can reduce the levels of IL-1β and TNF-α in OA-induced rat joint homogenates. These effects are comparable to those of the standard OA drug celecoxib. A dose of legetan leaf extract of 400 mg/kgBB showed the most significant anti-inflammatory effect.

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