https://doi.org/10.31925/farmacia.2026.2.15 **ORIGINAL ARTICLE**

ANTI-INFLAMMATORY ACTIVITIES OF PHYTOCOMPOUND POLYPEPTIDE-K AND ESSENTIAL OIL FROM *MOMORDICA CHARANTIA* (BITTER GOURD) SEEDS

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Abstract

Momordica charantia (MC), or bitter gourd, grows in tropical regions and has documented anti-diabetic, anti-ulcerogenic, antimicrobial, anti-tumour, anti-leukemic, and anti-inflammatory properties. This study evaluated the anti-inflammatory effects of polypeptide-K (PPK) and essential oil isolated from MC seeds in rat models of carrageenan-induced paw oedema and carrageenan-induced air pouch inflammation. In the paw oedema model, PPK and MC oil significantly reduced paw oedema volume, with effects comparable to indomethacin. In the air pouch model, PPK and MC oil suppressed total and absolute leukocyte, neutrophil, and monocyte counts, while PPK significantly reduced nitrite concentration. These findings suggest that PPK and MC oil inhibit acute inflammation by reducing leukocyte recruitment and nitrite production, and MC oil may additionally contribute through increased IL-10 during the late phase of inflammation. The results support the therapeutic potential of PPK and MC seed oil as candidate anti-inflammatory agents.

Rezumat

Momordica charantia (MC), cunoscută și sub denumirea de tărtăcuță amară (*bitter gourd*), crește în regiunile tropicale și prezintă proprietăți demonstrate antidiabetice, antiulcerogene, antimicrobiene, antitumorale, antileucemice și antiinflamatoare. Acest studiu a evaluat efectele antiinflamatoare ale polipeptidei-K (PPK) și ale uleiului esențial izolat din semințele de MC, utilizând modele experimentale la șobolani de edem plantar indus de caragenan și de inflamație de tip „*air pouch*" indusă de caragenan. În modelul de edem plantar, PPK și uleiul de MC au redus semnificativ volumul edemului, efectele fiind comparabile cu cele ale indometacinului. În modelul „*air pouch*", PPK și uleiul de MC au redus numărul total și absolut de leucocite, neutrofile și monocite, iar PPK a determinat o scădere semnificativă a concentrației de nitriți. Aceste rezultate sugerează că PPK și uleiul de MC inhibă inflamația acută prin reducerea recrutării leucocitelor și a producției de nitriți, iar uleiul de MC poate contribui suplimentar prin creșterea nivelului de IL-10 în faza tardivă a inflamației. Rezultatele susțin potențialul terapeutic al PPK și al uleiului din semințe de MC ca potențiali agenți antiinflamatori.

Keywords: *Momordica charantia*, polypeptide-K, essential oil, acute inflammation, paw edema

Introduction

In under-developed and developing nations, medicinal plants continue to play a significant role in medical systems. Many herbal medicines are extensively used in therapeutic practice, supported by empirical evidence. To develop new anti-inflammatory therapies, many natural compounds have already been evaluated in a variety of animal models (1). Numerous plant species have been studied scientifically to reveal bioactive chemicals with anti-inflammatory and health-promoting benefits (2). These compounds are increasingly used in treatment and prevention. Numerous herbs and plant extracts, including leaves (3, 4), essential oils, and active phytocompounds (5, 6), have been shown to effectively treat inflammation and related diseases (7).

Momordica charantia (MC), also known as bitter melon or bitter gourd, grows in tropical areas, including parts of the Amazon, East Africa, Asia, and the Caribbean, and is cultivated throughout South America as both food and medicine (8). Studies have shown that bitter melon fruit lowers blood glucose

and enhances cellular glucose uptake to promote insulin release (9, 10). The fruit has also demonstrated anti-ulcerogenic effects in ethanol-induced ulcerogenesis in rats (5), while polypeptide-K (PPK) has been isolated from MC seeds (11, 12). Seed extracts have shown broad-spectrum antimicrobial activity (13, 14). MC contains biologically active phytochemicals, including triterpenes, proteins, and steroids (8), and has traditionally been used as an anti-inflammatory, anti-leukemic, and anti-tumor medicinal herb (15). PPK isolated from MC seeds has been reported as a potent anti-diabetic (16) and anti-hypercholesterolemic agent (9). Clinical and nutritional studies also reported favorable effects of PPK supplementation (17, 18).

Previous studies mainly investigated the anti-inflammatory properties of whole MC fruit and seeds (7, 15). Given MC's traditional use in managing diabetes and inflammation, we hypothesized that both MC seed oil and PPK may exhibit potent anti-inflammatory activities. Notably, this study is the first to specifically evaluate the anti-inflammatory effects of purified PPK and essential oil derived from MC seeds in established experimental rat models of inflammation, providing novel insights into their potential therapeutic roles.

Materials and Methods

Chemicals

Polypeptide-K (PPK) compound and essential oil were supplied by Magna Bio-Laboratories Sdn. Bhd., Malaysia. The extraction method for PPK was described previously (12), and the extraction of MC seed oil followed prior work (7). Carrageenan, indomethacin, Griess reagent, rat IL-10 platinum ELISA reagent, sodium nitrate, sodium chloride, and other standard analytical-grade chemicals were used.

Experimental animals

Thirty-six male Sprague Dawley rats weighing 250-300 g were used in this study. Rats were randomly divided into six treatment groups. All procedures were approved by The Institutional Animal Care and Use Committee, Universiti Putra Malaysia (IACUC approval No. UPM/FPSK/PADS/BR-UUH/0038). The animals underwent an adaptation period of approximately two weeks before treatment. Rats were fed standard pellet diet and water *ad libitum*.

Carrageenan-induced paw edema model

Carrageenan-induced paw edema was assessed using methods described by Goh et al. (19) and Mamoun et al. (20) with slight modifications. Rats received oral administration of oil (50% and 100% (v/v) essential oil in tricaprylin (1.0mL/rat) or PPK (10 and 50 mg/kg) for four days. These doses were selected based on prior studies (5, 11, 16). Positive controls received 10 mg/kg indomethacin. Thirty minutes after treatment on day 4, 0.05 mL of 1% carrageenan suspension was injected intraplantarly into the right hind paw. Paw volume was measured with a Ugo Basile 7140 plethysmometer (Italy) before (V_0) and at 1, 2, 3, 4, and 5 h after carrageenan administration (V_T). The degree of inflammation was quantified from the change in paw volume ($V_T - V_0$).

$$\%\ inhibition = \frac{(V_T - V_0)_{Control} - (V_T - V_0)_{Treated}}{(V_T - V_0)_{control}} * 100$$

Carrageenan-induced air pouch model

Methods described by Fehrenbacher and McCarson (21) were used. Briefly, rats were grouped as in the paw edema experiment. On day 1, rats were anesthetized and 20 mL of sterile water was injected subcutaneously on the back to form pouches. Rats were pretreated orally for four days with oil or PPK [50% and 100% (v/v) essential oil, or 10 and 50 mg/kg PPK], while controls received 10 mg/kg indomethacin. On day 4, animals were re-anesthetized and injected with 2.0 mL sterile water; treatment continued to day 7. On day 7, 30 min after pretreatment, 5.0 mL of 0.5% carrageenan was injected into the pouch. Six hours later, rats were sacrificed and the pouch was washed with 10 mL normal saline. Exudates were collected on ice and volume was recorded as net exudate volume after subtraction of injected saline.

Interleukin-10 and nitrite determination

Collected exudates were centrifuged at 4900 rpm for 10 min at 4°C. The supernatant was used to detect interleukin-10 using a commercial kit (22) and nitric oxide indirectly by the Griess reaction, read on an ELISA plate reader at 548 nm (23). The sediment was resuspended in 2.0 mL saline for total cell count using an automated cell counter and for differential cell count by slide smear.

Statistical analysis

All data were expressed as mean ± SEM. One-way analysis of variance followed by Tukey's post hoc test was performed using GraphPad Prism 5 software. Values of $p < 0.05$ were considered statistically significant.

Results and Discussion

Carrageenan-induced paw edema in rats

In carrageenan-induced paw edema, the negative control group showed a gradual increase in edema volume, with the maximum mean paw volume observed at 60 minutes after carrageenan injection (0.8383 ± 0.10849 mL; Table I). Significant reductions in paw edema volume at 60 minutes were observed for the positive control group, 50 mg/kg PPK, 50% (v/v) essential oil, and 100% (v/v) essential oil when compared with the negative control ($p < 0.05$). The 50 mg/kg PPK group showed the highest percentage inhibition of edema at 60 minutes (74.75%), followed by 10 mg/kg PPK (63.02%), 100% MC oil (59.64%), 50% MC oil (56.06%), and indomethacin

(31.21%) (Table II). The 33 % inhibition by Indomethacin is low but it is between the rance of its anti-inflammatory activity as demonstrated by Cong et al (24), they reported Indomethacin has 33 to 55% inhibition at 10mg/kg. Newer NSAIDs may have more potent inhibition such as Diclofenac or piroxicam (19, 23). PPK may exert its activity early but NSAID indomethacin may be potent at the late phase. These results suggest that 50 mg/kg PPK was particularly effective during the early phase of inflammation and may reduce vascular permeability and fluid infiltration by affecting inflammatory mediator release (25). Carrageenan-induced inflammation is associated with the early release of histamine, serotonin, and bradykinin, followed by later prostaglandin and nitric oxide production through COX-2 and iNOS pathways (1, 26). As previously reported (27), many natural products inhibit inflammation through this pathway.

Table I

Effects of Polypeptide-K (PPK) and essential oil of seeds of *Momordica charantia* on mean paw volume in carrageenan-induced paw edema

	Paw Edema (mL)						
Group	**0 min**	**30 min**	**60 min**	**120 min**	**180 min**	**240 min**	**300 min**
Negative Control	0.4650 ± 0.09629^{ax}	0.7017 ± 0.09210^{ay}	0.8383 ± 0.10849^{ay}	0.2080 ± 0.11438^{ax}	0.2767 ± 0.12771^{ax}	0.3550 ± 0.17489^{ax}	0.2550 ± 0.08917^{ax}
Positive Control	0.3667 ± 0.138360^{ax}	0.3067 ± 0.098650^{bx}	0.5767 ± 0.161280^{ay}	0.2667 ± 0.066370^{ax}	0.1933 ± 0.005162^{ax}	0.0883 ± 0.073680^{ax}	0.1317 ± 0.028920^{ax}
10 mg/kg PPK	0.2467 ± 0.09153^{ax}	0.2317 ± 0.11998^{bcx}	0.2583 ± 0.11347^{bx}	0.1033 ± 0.04169^{ax}	0.2033 ± 0.09945^{ax}	0.3433 ± 0.09611^{ax}	0.3567 ± 0.12352^{ax}
50 mg/kg PPK	0.3250 ± 0.07173^{ax}	0.3300 ± 0.10023^{bcx}	0.2117 ± 0.06426^{bx}	0.3900 ± 0.08185^{ax}	0.3400 ± 0.09630^{ax}	0.2100 ± 0.06481^{ax}	0.2667 ± 0.09752^{ax}
50% MC Oil	0.2433 ± 0.11081^{ax}	0.4050 ± 0.12307^{abcx}	0.3683 ± 0.10806^{bx}	0.3183 ± 0.16412^{ax}	0.3350 ± 0.09394^{ax}	0.1800 ± 0.15776^{ax}	0.3550 ± 0.13458^{ax}
100% MC Oil	0.5033 ± 0.19761^{ax}	0.1350 ± 0.07680^{cx}	0.3383 ± 0.09673^{bx}	0.2450 ± 0.05445^{ax}	0.2850 ± 0.12987^{ax}	0.2050 ± 0.11310^{ax}	0.2850 ± 0.08156^{ax}

Values are mean ± S.E.M. (n = 6/group). $^{a-c}$Significant difference ($p < 0.05$) of different superscripts when compared to means in the same column. $^{x-y}$Significant difference ($p < 0.05$) of different superscripts when compared to means in the same row. Positive control = rats received 10 mg/kg indomethacin; negative control = rats received dosed vehicle (5 mL/kg DH_2O). MC oil = essential oil from seeds of Momordica charantia.

Table II

Percentage inhibition of carrageenan-induced paw edema at 60 minutes

Group	**Percentage inhibition (%)**
Negative Control	-
Positive Control	31.21
10 mg/kg PPK	63.02
50 mg/kg PPK	74.75
50% MC Oil	56.06
100% MC Oil	59.64

Values are mean ± S.E.M. (n = 6/group. Positive control = rats received 10 mg/kg Indomethacin; Negative control = rats received dosed vehicle (5 mL/kg DH_20). MC oil = Essential oil from seeds of *Momordica charantia.*

Carrageenan-induced air pouch

Total exudate volume did not differ significantly between treatment groups (Table III). However, total leukocyte count was significantly reduced in the 50 mg/kg PPK group and in both MC seed oil groups (Table IV). In absolute leukocyte counts, neutrophils were significantly lower in all treatment groups compared with the negative control, whereas monocyte reduction was more evident in the positive control and 50 mg/kg PPK groups (Table V). The strongest inhibition of leukocyte recruitment was observed with 50% MC seed oil. These findings indicate that MC oil may be more effective in the late phase of inflammation, likely through suppression of inflammatory mediator synthesis, cell migration, and vascular leakage (4,28). Because exudates were collected 6 h after carrageenan induction, this model mainly reflects late acute inflammatory events. Indeed, several studies have shown anti-inflammatory activities via this pathway (29,30). As the total volume was not statistically significant (Table III), even for the positive control group, this may reflect variability within the model or the specific parameters measured. Future studies with larger sample sizes may further clarify these effects must be performed.

Table III

Total exudate volume of Polypeptide-K (PPK) and essential oil of seeds of *Momordica charantia* in carrageenan-induced air pouch

Group	**Mean volume exudate (mL)**
Negative Control	2.013 ± 0.2654^{a}
Positive Control	1.7535 ± 0.2186^{a}
10 mg/kg PPK	1.930 ± 0.3467^{a}
50 mg/kg PPK	2.433 ± 0.5258^{a}
50% MC Oil	2.262 ± 0.2554^{a}
100% MC Oil	1.940 ± 0.3617^{a}

Values are mean ± S.E.M. (n = 6/group); $^{a-c}$Significant difference ($p < 0.05$) of different superscripts when compared to means in the same column. Positive control = rats received 10 mg/kg Indomethacin; Negative control = rats received dosed vehicle (5 mL/kg DH_20). MC oil = Essential oil from seeds of *Momordica charantia.*

Table IV

Effects of Polypeptide-K (PPK) and essential oil of seeds of *Momordica charantia* on mean total leukocytes in carrageenan-induced air pouch

Group	Mean total leukocytes count (10^3/µL)
Negative Control	60.967 ± 10.297[a]
Positive Control	39.067 ± 4.312[a]
10 mg/kg PPK	38.050 ± 6.044[a]
50 mg/kg PPK	27.225 ± 7.035[b]
50% MC Oil	20.967 ± 5.283[b]
100% MC Oil	26.433 ± 4.584[b]

Values are mean ± S.E.M. (n = 6/group); [a-c]Significant difference ($p < 0.05$) of different superscripts when compared to means in the same column; Positive control = rats received 10 mg/kg Indomethacin; Negative control = rats received dosed vehicle (5 mL/kg DH_20). MC oil = Essential oil from seeds of *Momordica charantia*

Table V

Effects of Polypeptide-K (PPK) and essential oil of seeds of *Momordica charantia* on mean absolute leukocyte count in carrageenan-induced air pouch

Group	Neutrophils (10^3/µL)	Monocytes (10^3/µL)
Negative Control	43.316 ± 8.851[a]	11.590 ± 1.816[a]
Positive Control	22.643 ± 2.606[b]	5.4213 ± 0.648[b]
10 mg/kg PPK	20.382 ± 3.14[b]	7.4438 ± 1.141[a]
50 mg/kg PPK	15.776 ± 4.073[b]	4.0161 ± 1.114[a]
50% MC Oil	12.603 ± 3.131[b]	4.0020 ± 1.315[a]
100% MC Oil	14.787 ± 2.723[b]	5.6330 ± 1.515[a]

Interleukin-10 concentration

No statistically significant differences in IL-10 concentration were observed among groups, although the 50% (v/v) MC seed oil group showed the highest value (Table VI). IL-10 is an anti-inflammatory cytokine that suppresses pro-inflammatory cytokine synthesis and inflammatory cell migration (26, 31). Previous in vitro work showed that MC juice can up-regulate IL-10 secretion (32). The higher IL-10 level observed with 50% MC oil may indicate an anti-inflammatory contribution through increased anti-inflammatory signalling and reduced iNOS/COX-2 pathway activity (33), although the late sampling time may have limited detection of transient IL-10 responses.

Table VI

Determination of interleukin-10 (IL-10) and nitrite from exudate collection in carrageenan-induced air pouch

Group	Mean Interleukin-10 (pg/mL)	Mean Nitrite concentration (µmol/g)
Negative Control	402.623 ± 80.701[a]	65.798 ± 16.204[a]
Positive Control	240.667 ± 23.212[a]	23.748 ± 6.550[b]
10mg/kg PPK	335.152 ± 121.031[a]	28.530 ± 11.174[a]
50mg/kg PPK	253.942 ± 65.733[a]	14.352 ± 3.528[b]
50% MC Oil	483.377 ± 84.818[a]	55.919 ± 9.809[a]
100 % MC Oil	338.848 ± 33.520[a]	25.798 ± 5.410[a]

Values are mean ± S.E.M. (n = 6/group); [a-c]Significant difference ($p < 0.05$) of different superscripts when compared to means in the same column. Positive control = rats received 10 mg/kg Indomethacin; Negative control = rats received dosed vehicle (5 mL/kg DH_20). MC oil = Essential oil from seeds of *Momordica charantia.*

Nitrite concentration

Significant reductions in nitrite concentration were observed in the positive control group and in the 50 mg/kg PPK group (Table VI). Nitric oxide is rapidly converted into nitrite and nitrate; therefore, nitrite is commonly measured as an indicator of nitric oxide production during inflammation (23). Inducible nitric oxide synthase is a key therapeutic target in inflammatory disease because it contributes to vascular permeability and inflammatory signalling (25, 30). The reduction in nitrite concentration suggests that 50 mg/kg PPK may suppress inflammatory mediator signalling and reduce endothelial permeability in acute inflammation.

Results from our current and previous studies Abu Bakar *et al*. (5,11); Yong *et al*. (9); Ahmad *et al*. (16) and Yong *et al*. (17) suggest that PPK and MC seed oil have potent biomedical activities. We have yet can conclude the mechanism/s of action of both PPK and MC oil. Indeed, future studies of the exact mechanism/s of anti-inflammation must be performed to further elucidate the exact molecular mechanism and a complete toxicological assessment for the safety of the compounds (31). Furthermore, increasing the sample size in future studies will be essential to

enhance the statistical power and robustness of the findings. These findings highlight the potential for PPK and MC Oil in the development of new and safe anti-inflammatory agents as previously reported the brief toxicological evaluations of PPK and it is devoid of any side effects (33). The current study's limitations, including the relatively small sample size and short duration, may have impacted the ability to detect certain effects. Addressing these limitations in future research will provide more definitive conclusions (34, 35).

Conclusions

In conclusion, PPK and the essential oil that is produced from MC seeds have the ability to reduce the volume of paw oedema and may also prevent acute inflammation by lowering the number of leukocytes and nitrite generation. The oil's ability to suppress nitrite and increase IL-10 demonstrated that it could prevent acute inflammation in its late stages, with comparable effectiveness to the control NSAID, indomethacin.

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Availability of data and materials

The data generated in the present study are included in the tables of this article.

Ethics approval and consent to participate

All experimental procedures were approved by The Institutional Animal Care and Use Committee, Universiti Putra Malaysia (approval No. UPM/FPSK/PADS/BR-UUH/0038).

AI use disclosure

During the preparation of this manuscript, the author(s) used ChatGPT for editing assistance and language improvement, specifically to improve spelling, grammar, word choice, readability, and clarity. The author(s) reviewed and revised all outputs from these tools and take(s) full responsibility for the final content of the work.

Conflict of interest

The authors declare no conflict of interest.

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