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Preventive Effect of Boiogito, a Japanese Traditional Herbal Medicine, on Osteophyte Formation in a Rat Model of Knee Osteoarthritis.

Takayuki Okumo[1,2)], Tokito Tatsuo[1,2)], Kanako Izukashi[1,2)], Hideshi Ikemoto[1)], Naoki Adachi[1)], Atsushi Sato[2)], Koji Kanzaki[2)], Masataka Sunagawa[1)]

1. Department of Physiology, Showa Medical University Graduate School of Medicine.
2. Department of Orthopedic Surgery, Showa Medical University Fujigaoka Hospital

COI disclosure

We have nothing to disclose in this study.

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Presenting author: Takayuki Okumo

Introduction

Knee Osteoarthritis (KOA)

- A degenerative joint disease that significantly impairs patients' quality of life.
  - Affects approximately 595 million individuals worldwide (7.6% of the global population).

Secondary KOA

- Caused by identifiable factors such as trauma, infection, or hematologic disorders.
- Accounts for approximately 13% of all KOA cases.
- Some patients experience a more rapid progression of the disease.

Current Therapeutic Strategies

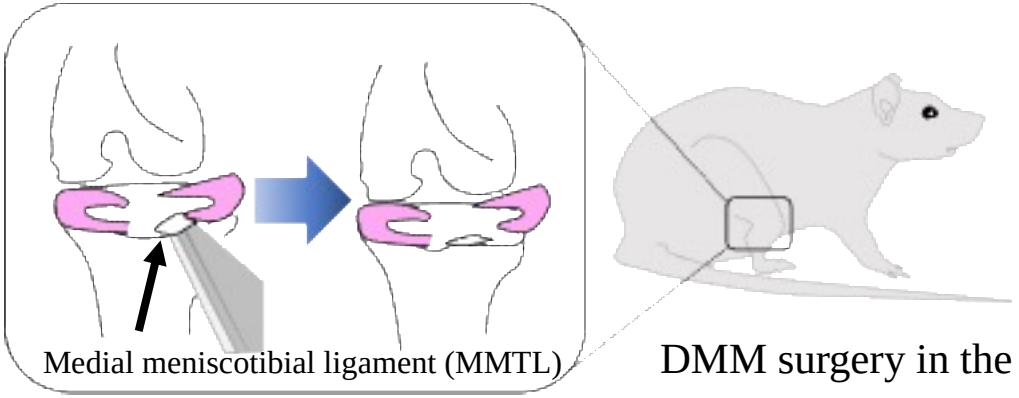
- No established, evidence-based treatment is available to prevent KOA progression.
- Herbal medicine is being explored as a potential preventive intervention

Introduction

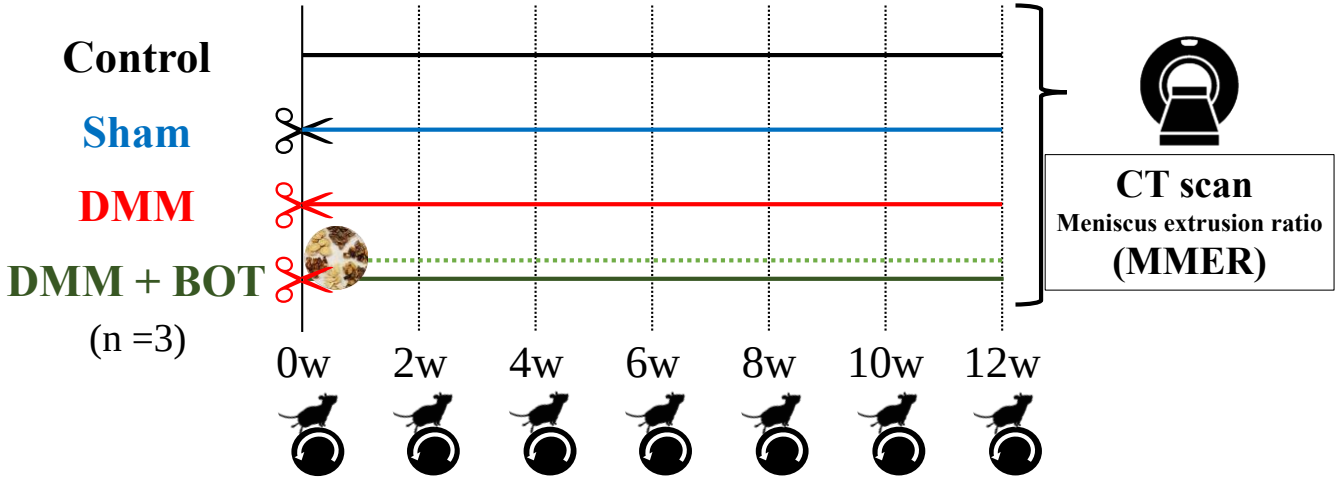
Boiogito (BOT)

- A traditional Japanese herbal medicine, known in Chinese as Fangji Huangqi Tang, originally documented in the 3rd century.
- Traditionally used to alleviate joint effusion and pain, particularly in the lower extremities.
- Clinical observations indicate improvement in knee pain, joint effusion, and stair-climbing ability.
- In vivo studies demonstrate that BOT suppresses KOA progression in a meniscus injury-induced secondary KOA rat model over a 4-week period.
- **The long-term effectiveness of BOT in preventing KOA progression remains to be elucidated.**

Study Protocol



DMM surgery in the right knee joint

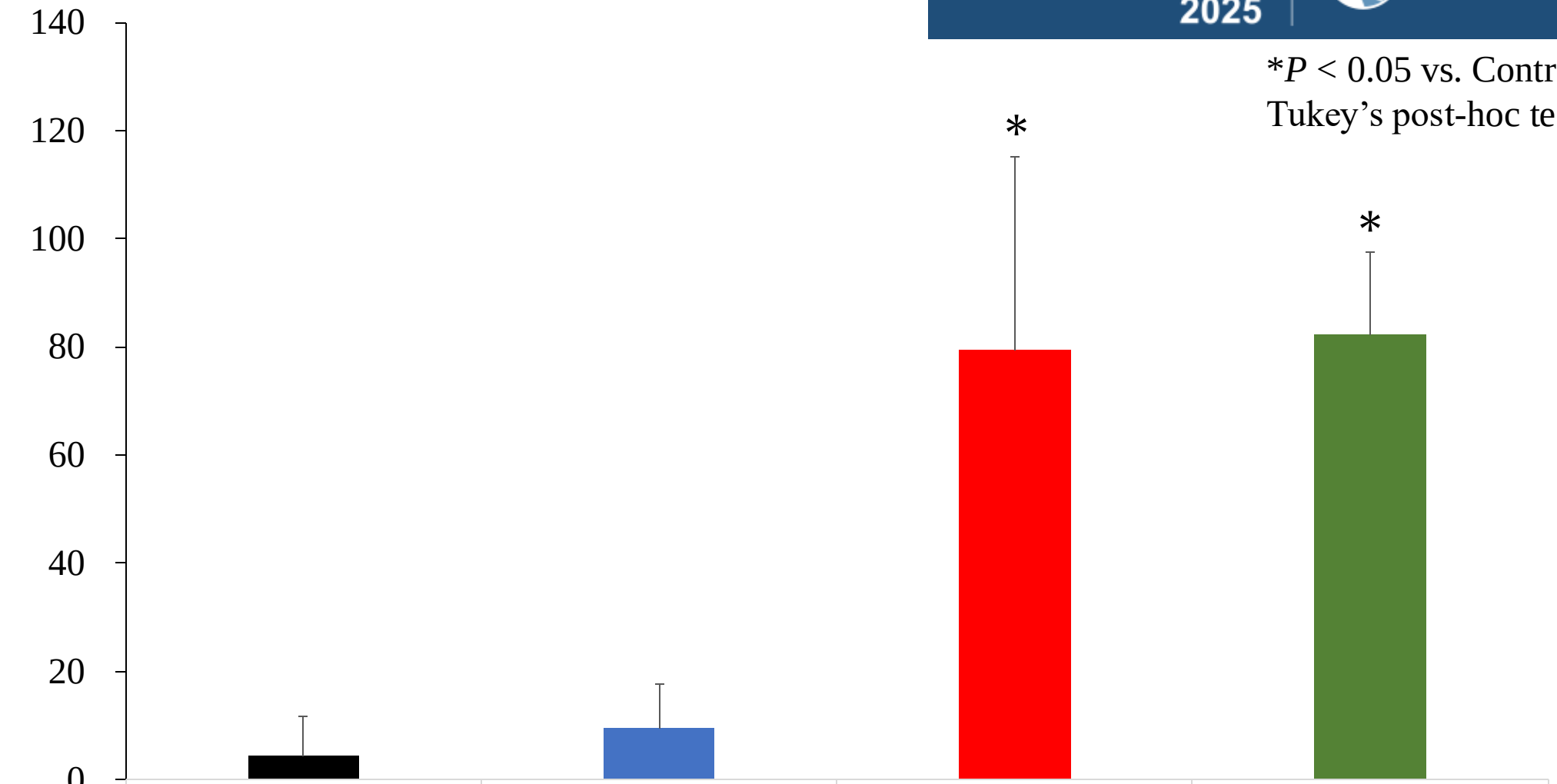


：Oral administration of BOT

：Rotarod test

Right knee joint
Histological analysis
Toluidine blue staining
➡OARSI score

- Animal: Ten-week-old male Wistar rats
- KOA induction
  - Destabilization of the medial meniscus (DMM)
- Groups (n = 3)
  - Control: No surgery, no treatment
  - Sham: Surgery without transecting MMTL, no treatment
  - DMM: DMM surgery, no treatment
  - DMM + BOT: DMM surgery, oral administration of BOT
- Data curation and analysis
  - Medial meniscus extrusion ratio (MMER): CT scan
  - Pain, motor dysfunction: Rotarod test
  - KOA progression：Histological analysis
    - Toluidine blue staining
    - Osteoarthritis Research Society International recommending scoring system (0–24 points)
- Statistical analysis
  - JMP Pro Ver. 17.0
  - Data provision: Mean ± Standard deviation
  - Tukey’s post-hoc test
  - Significance level: less than 5%

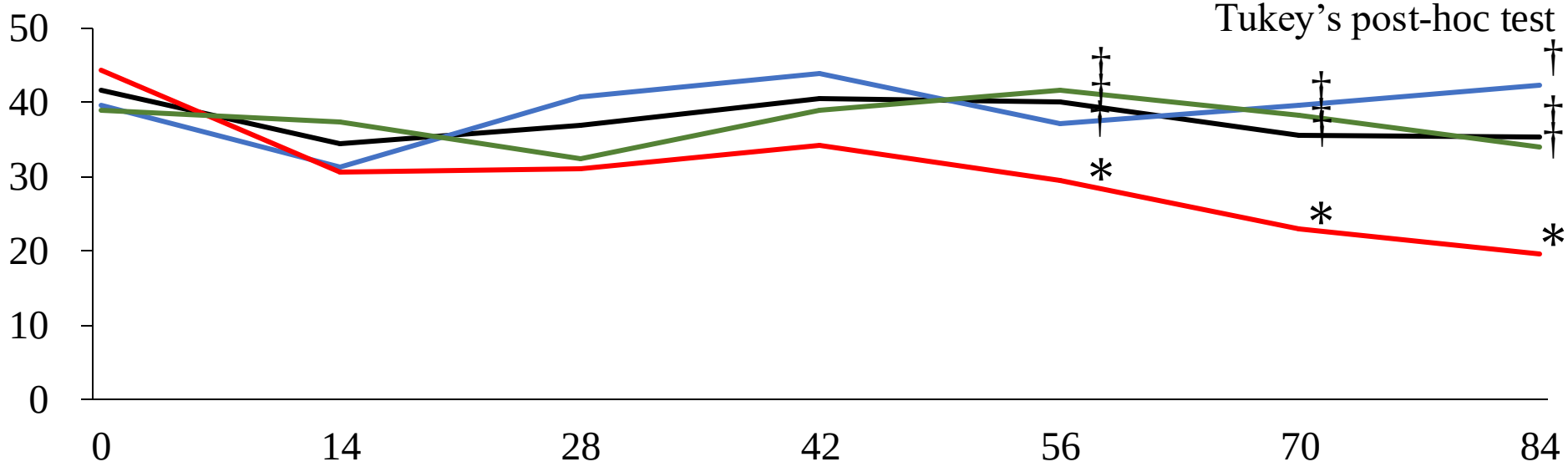


*P < 0.05 vs. Control group
Tukey's post-hoc test

	Control	Sham	DMM	DMM + BOT
MMER	4.3	9.4	79.5	82.3

Rotarod test

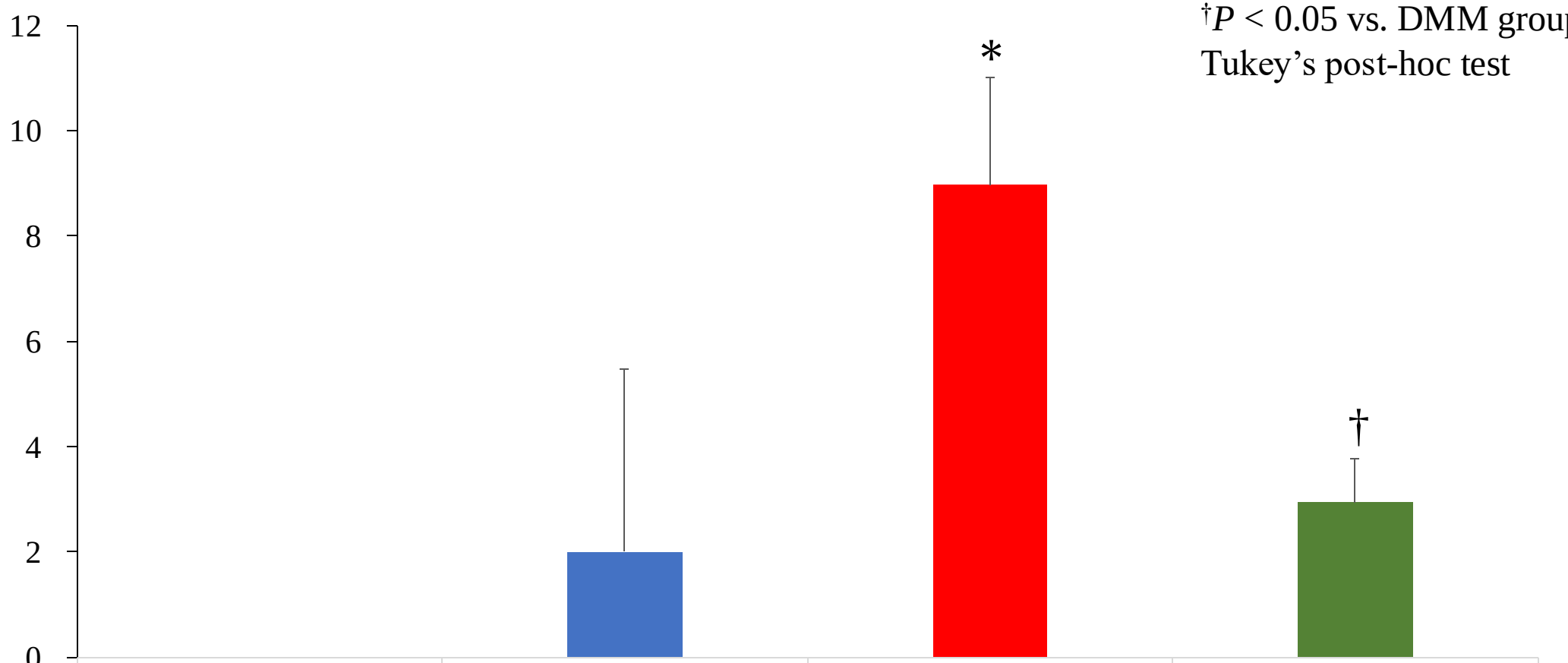
*P < 0.05 vs. Control group
†P < 0.05 vs. DMM group
Tukey's post-hoc test



	0	14	28	42	56	70	84
Control	41.6	34.4	37.0	40.6	40.0	35.6	35.4
Sham	39.7	31.3	40.7	43.9	37.2	39.6	42.4
DMM	44.3	30.6	31.1	34.3	29.5	23.0	19.7
DMM + BOT	39.0	37.3	32.4	39.0	41.6	38.2	34.1

Control Sham DMM DMM + BOT

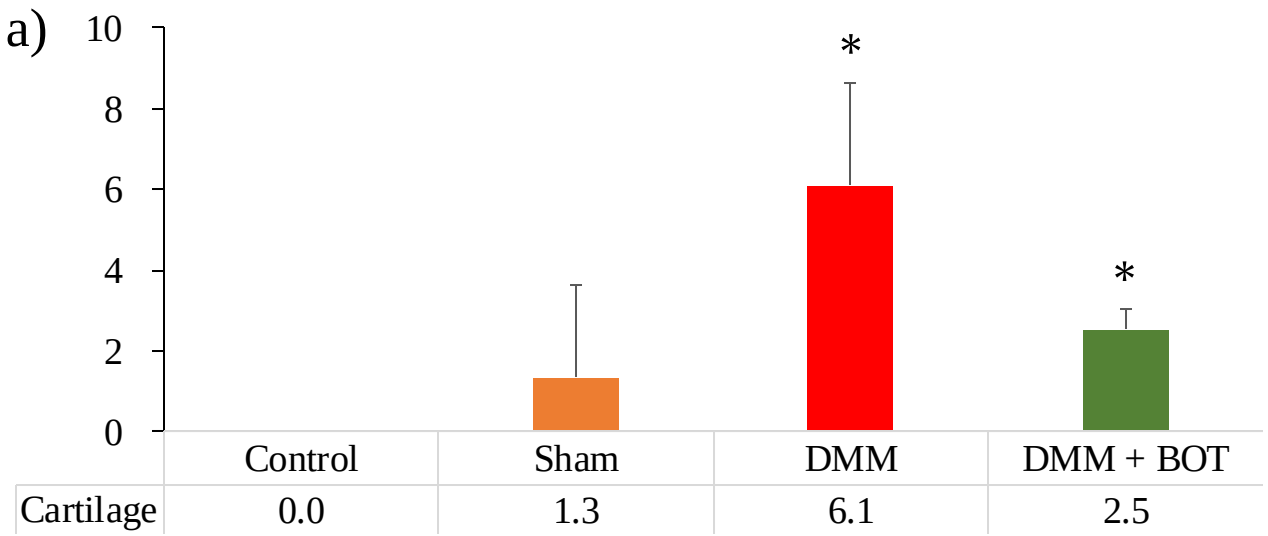
OARSI score



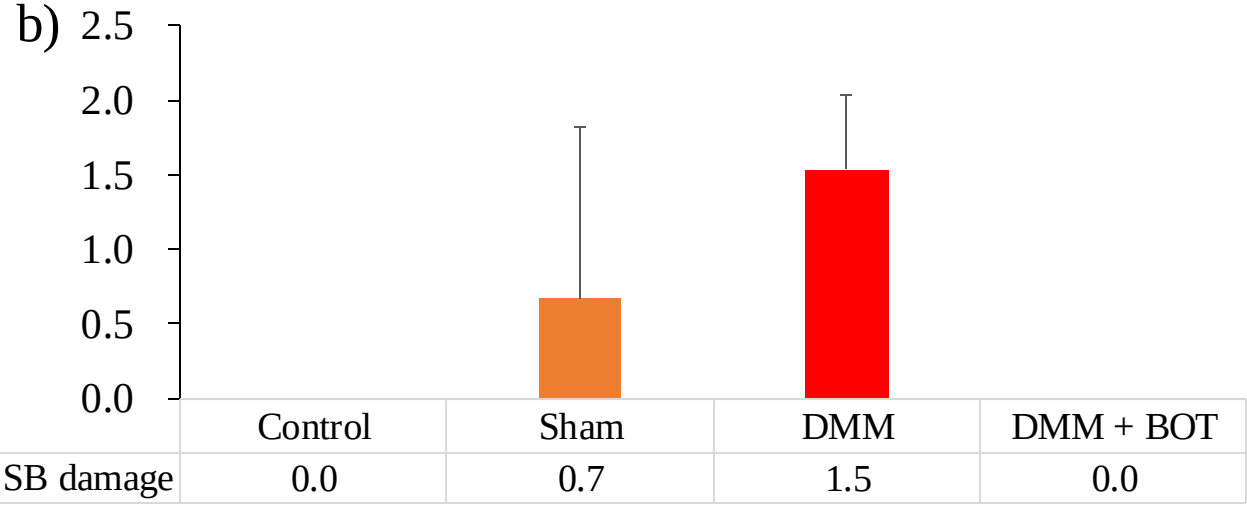
*P < 0.05 vs. Control group
†P < 0.05 vs. DMM group
Tukey's post-hoc test

	Control	Sham	DMM	DMM + BOT
OARSI score	0.0	2.0	9.0	2.9

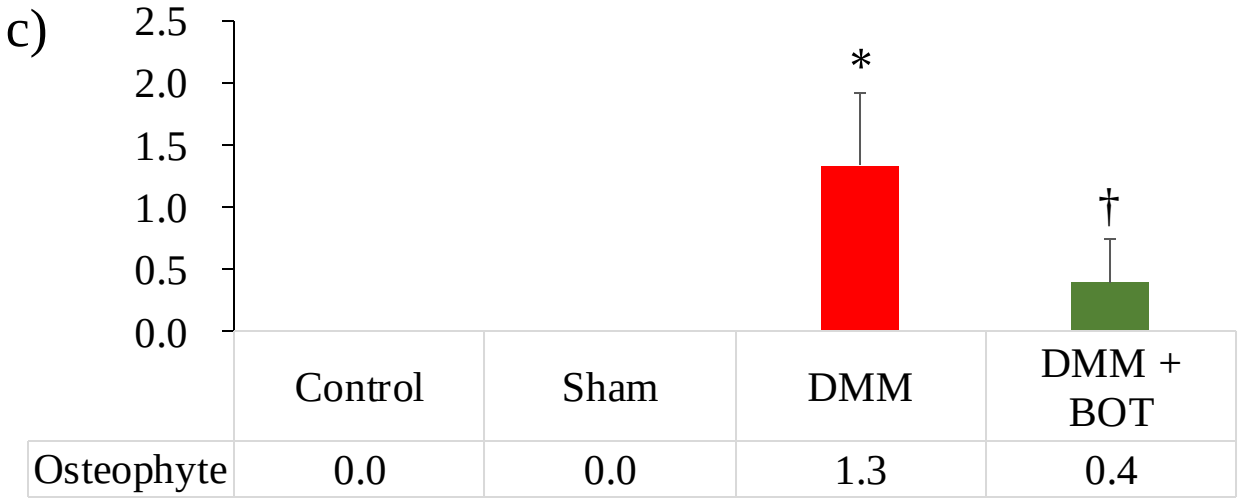
Subscale of the OARSI score



	Control	Sham	DMM	DMM + BOT
Cartilage	0.0	1.3	6.1	2.5



	Control	Sham	DMM	DMM + BOT
SB damage	0.0	0.7	1.5	0.0



	Control	Sham	DMM	DMM + BOT
Osteophyte	0.0	0.0	1.3	0.4

Subscale of the OARSI score

a) Cartilage degradation score (0–15 points), b) Subchondral bone damage score (0–4 points), c) Osteophyte formation score (0–5points). *$P < 0.05$ vs. Control group, †$P < 0.05$ vs. DMM group based on the Tukey's post-hoc test.

Discussion

Medial Meniscus Dysfunction

- The hoop function of the medial meniscus is impaired.
- As a result, contact pressure on the articular cartilage and subchondral bone increases by up to 200% compared to the healthy knee.

DMM Rat Model

- The anterior medial meniscotibial ligament (MMTL) is transected.
- Although the meniscus body remains structurally intact, the hoop function is completely lost.
- This model closely replicates the clinical condition of a medial meniscus posterior root tear (MMPRT). It exhibits hallmark features of KOA progression, including cartilage degeneration, subchondral bone damage, and osteophyte formation.

Discussion

Osteophyte Formation and Knee Symptoms

- Osteophytes are formed through abnormal bone metabolism triggered by inflammatory responses within the knee joint.
- Paracrine signaling from the synovium is considered one of the key factors in inducing new bone formation at the margins of the subchondral bone.
- Osteophytes contribute to knee pain and functional impairment.

Therapeutic Effect of BOT *In Vivo*

- In the present study, BOT administration suppressed osteophyte formation and mitigated pain-related motor dysfunction in the DMM rat model.
- These findings suggest that early administration of BOT may be effective in preventing KOA progression and associated knee dysfunction.

Conclusion

- This study demonstrated that oral administration of Boiogito (BOT), a traditional Japanese herbal medicine, effectively suppressed osteophyte formation, alleviated pain-related motor dysfunction, and reduced cartilage degeneration in a rat model of secondary knee osteoarthritis.

- These findings suggest that early intervention with BOT may represent a promising therapeutic strategy to prevent structural joint deterioration and functional decline associated with the progression of KOA.

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