

## Anti-arthritic activities of the extract of radiation mutant *Perilla frutescens* var. *crispa* in CAIA

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### 1. Introduction

In this study, we determined the anti-arthritic effects of the radiation mutant *Perilla frutescens* var. *crispa* leaf extract (SFE-M) and wild type leaf extract (SFE-W), both prepared by supercritical carbon dioxide (SC-CO<sub>2</sub>) extraction, on the development of collagen antibody-induced arthritis (CAIA) in Balb/c mice. Experimental animals were randomly divided into four groups: normal, CAIA, CAIA + SFE-M (100 mg/kg/day), and CAIA + SFE-W (100 mg/kg/day) and respective treatments were administered via oral gavage once per day for 4 days. Mice treated with SFE-M developed less severe arthritis than the control CAIA mice. They showed significantly improved arthritic score, paw volume, and paw thickness compared to the control CAIA mice from days 3 through 7. Furthermore, histopathological examination of ankle for inflammation showed that infiltration of inflammatory cells and edema formation were reduced by SFE-M treatment. Similarly, neutrophil to lymphocyte ratio (NLR) in whole blood was lower in mice treated with SFE-M by 37% compared to the control CAIA mice. However, SFE-W didn't show any significant result compared to the control CAIA group. Taken together, SFE-M treatment delays the onset of the arthritis and alleviates the manifestations of arthritis in CAIA mice.

### 2. Methods and Results

#### 2.1 Preparation of SFE-M and SFE-W

In this study, leaf extracts from radiation mutant *P. frutescens* var. *crispa* and wild type were acquired using SC-CO<sub>2</sub> method. Fig. 1 shows the compositions of the two extracts. Isoegomaketone(IK) content was approximately 7-fold higher in SFE-M compared with SFE-W. IK content was  $76.0 \pm 0.7$  mg/g and  $10.8 \pm 0.3$  mg/g in SFE-M and SFE-W, respectively.

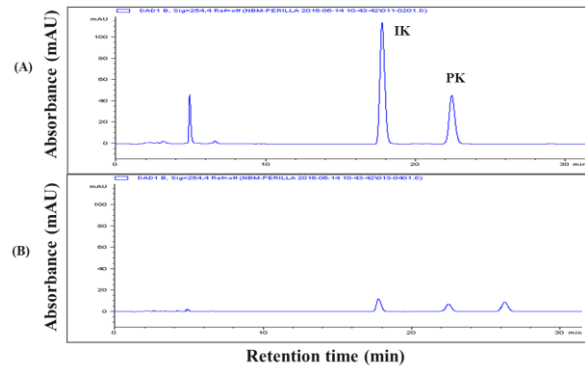


Fig. 1. HPLC chromatograms. (A) SFE-M, (B) SFE-W

#### 2.2 Effect of SFE-W and SFE-M treatment on the development of RA in CAIA model

Whether SFE-W treatment by oral administration prevented initiation of disease in Balb/c mice with CAIA was investigated. SFE-M-treated mice developed less severe arthritis. Both redness and swelling of joints were induced in the control CAIA group, but those arthritic symptoms were significantly attenuated in SFE-M-treated group (100 mg/kg). Histopathological examinations also indicated that SFE-M treatment reduced synovial hyperplasia and the infiltration of inflammatory cells in the joint space. Mean histopathological arthritic score of CAIA-group, SFE-M-treated group, and SFE-W-treated group were  $2.33 \pm 0.82$ ,  $0.00 \pm 0.00$ ,  $1.00 \pm 0.89$ , respectively (Table I). The weight of mice was reduced from days 3 through 6 in all CAIA-induced groups except the corn oil group.

Table I: Histopathological scores of the groups

Organ	Group	Corn oil	CAIA	CAIA+ SFE-M	CAIA+ SFE-W
Ankle joint	Inflammation	-	6	0	6
		±	0	1	0
		+	0	2	0
		++	0	3	0
		+++	0	4	0

Grade- -:normal ±: minimal, +: mild, ++: moderate, +++: marked  
No. of examined : 6/group

### 3. Conclusions

There are many reports about anti-arthritic medicinal plants, which have been tested in animal and human studies [1-4]. Radiation-induced mutant *P. frutescens* var. *crispa* used in this study has higher anti-inflammatory activities and its extract prepared by supercritical carbon dioxide extraction also has a good potential as anti-arthritic medicinal plant source. To our knowledge, this is the first report that describes the radiation-induced plant mutants containing higher anti-arthritic properties compared to wild-type.

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