ORIGINAL ARTICLE

Effects of sesame oil in the model of adjuvant arthritis

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Abstract

OBJECTIVES: The goal of this study was to evaluate the effect of sesame oil on functional damage induced by adjuvant arthritis (AA) and on changes of selected biochemical parameters reflecting oxidative tissue injury.

DESIGN: *Mycobacterium butyricum* in incomplete Freund's adjuvans was intradermally administered to Lewis male rats. Hind paw edema and endothelium-dependent relaxation of the aorta were determined on day 28. Further, plasmatic levels of TBARS, gamma-glutamyltransferase (GGT) activity in the joint and spleen tissues, level of protein carbonyls and total antioxidant capacity (TAC) in plasma, as well as activity of the lysosomal enzyme N-acetyl-glucosaminidase (NAGA) in serum were assessed. The effect of sesame oil (SO, 1ml/kg, daily oral administration) was evaluated on day 28.

RESULTS: The beneficial effect of sesame oil on markers of oxidative stress accompanying AA was demonstrated by decrease of plasma TBARS and decrease of GGT activity in the joint and spleen tissues. Level of protein carbonyls, TAC in plasma and activity of NAGA in serum and in the kidney were improved, yet not significantly. In the hind paw edema the maximal increase was found on day 28 of AA, and in the same time we observed a significant decrease of aortic endothelium-dependent relaxation. Administration of SO resulted in mild, non-significant decrease of hind paw swelling and in significantly increased acetylcholine-evoked relaxation.

CONCLUSION: We conclude that SO has beneficial effects on oxidative stress induced biochemical changes occurring in AA, moreover it improves endothelium-dependent relaxation of the aorta and tends to decrease hind paw edema.

INTRODUCTION

SO is a component of the traditional health food in oriental countries. The oil was reported to have high antioxidant activity (Baba *et al.* 1998; Namiki, 2007), which contributes to its effects against increased blood pressure, hyperlipidemia and lipid peroxidation (Sankar *et al.* 2005). The principal antioxidant component of SO is sesaminol (Osawa *et al.* 1990), however phenol, sesamin, sesamol, sesamolin and relatively small amounts of tocopherol contribute to its oxidative stability (White, 1992). As oxidative stress is known to contribute to the pathogenesis of chronic inflammatory diseases such as rheumatoid arthritis, utilization of antioxidant activity of SO might be of importance in anti-arthritic therapy.

The present study was undertaken to assess the effect of SO on functional damage induced by AA

Abbrevations

AA	adjuvant arthritis
GGT	gamma-glutamyltransferase
HPV	hind paw volume
NAGA	N-acetyl-glucosaminidase
SEM	standard error of mean
SO	sesame oil
TAC	total antioxidant capacity
TBARS	thiobarbituric acid reactive substances
CYP	cytochrome P450

and on changes of selected biochemical parameters reflecting oxidative tissue injury.

MATERIAL AND METHODS

After approval by the local ethical committee, AA was induced in male Lewis rats (150–170 g) by a single intradermal injection of heat-inactivated *Mycobacterium butyricum* in incomplete Freund's adjuvant. The experiments included healthy intact rats (C), arthritic rats (AA), and arthritic rats treated with SO (AA+SO), with 8 rats in each group. SO was administered daily (1 ml/kg body weight, orally) from the day of bacterial inoculation. On day 28 the animals were sacrificed and the following biochemical parameters were measured: TAC in plasma by the 2,2`-azinobis(3-ethylbenzothiazoline 6-sulfonate) assay (Rice-Evans & Miller, 1994), protein carbonyl groups in plasma using enzyme linked immunosorbent assay, as described by Buss *et al.* (1998), TBARS in plasma spectrophotometrically at 535 nm (Brown & Kelly, 1996), activity of GGT in spleen and hind paw joint homogenates spectrophotometrically (Bauerova *et al.* 2006). NAGA activity in plasma was assayed according to Barrett & Heath (1977). Further, changes in the hind paw volume (HPV), as the percentage of increase in HPV on day 28 compared to day 0, were evaluated (Bauerova *et al.* 2006, 2008). Endothelium-dependent relaxation of the isolated aorta was determined under isometric conditions (Sotnikova *et al.* 2001) as the response of phenylephrine precontracted rings to acetylcholine.

Statistical analysis was assessed by ANOVA followed by Student's t-test; P<0.05 were considered significant, $p<0.01$ very significant and $p<0.001$ extremely significant. The arthritic group was compared to healthy control animals (*), the treated AA groups were compared to the untreated AA group (+).

Table 1. Markers of oxidative stress in control rats, rats with adjuvant arthritis (AA), and rats with adjuvant arthritis treated with sesame oil (AA+SO). Values are means ± SEM of 8 animals. *$p < 0.05$, ***$p < 0.001$ AA *versus* C, +$p < 0.05$ AA *versus* AA+SO.

Parameters measured	Control	AA	AA + SO
TBARS in plasma (nmol/ml)	12.0 ± 0.78	16.4 ± 1.61 ***	13.75 ± 1.39 +
GGT activity in the joint (nmol p-nitroaniline/ min/g wet weight)	14.08 ± 2.44	23.46 ± 0.82 ***	15.85 ± 2.91 +
GGT activity in the spleen (nmol p-nitroaniline/ min/g wet weight)	14.02 ± 2.77	84.54 ± 8.59 ***	65.78 ± 4.69
Protein carbonyls in plasma (nmol/mg protein)	1.12 ± 1.19	10.0 ± 0.76 ***	9.61 ± 0.62
TAC in plasma (mmol/l)	0.09 ± 0.02	0.04 ± 0.02 *	0.05 ± 0.01
NAGA activity in serum (µg 4-nitrophenol/ min/mg protein)	0.044 ± 0.003	0.066 ± 0.003 ***	0.062 ± 0.002

RESULTS AND DISCUSSION

As shown in ***Table 1***, AA induced changes in all biochemical parameters tested. The beneficial effect of SO was demonstrated by a significant decrease in plasma TBARS and decrease in GGT activity in joint and spleen tissue homogenates. Levels of protein carbonyls, TAC in plasma and activity of NAGA in serum were slightly improved, yet not significantly.

A maximal increase in HPV (***Fig.1***) and significant decrease in aortic endothelium-dependent relaxation was found on day 28 of AA (***Fig. 2***). Administration of SO resulted in mild, non-significant decrease in HPV and in significantly increased acetylcholine-evoked relaxation.

Changes in biochemical parameters measured, as well as impaired endothelial function and hind paw swelling confirmed that besides inflammation also oxidative stress is involved in AA establishment. Further, our results are indicative of beneficial effects of SO in AA. This is in good agreement with results of other authors who found antioxidant activity of SO (Saif *et al.* 2006) and its individual components, e.g. lignan sesamolin (Kang *et al.* 1998). The mechanism of antioxidant effect of sesaminol, the major antioxidant component of SO, consists in increase of vitamin E levels in plasma and tissues by inhibition of CYP enzymes, which are responsible for vitamin E decomposition (Yamashita *et al.* 2007). Another component of SO – sesamin is probably responsible for antiinflammatory activity of SO (Willis, 1981; Mathias & Dupont, 1985).

In our experiments we observed impaired endothelial function of the aorta of rats with AA. AA-induced endothelial dysfunction was reported also by Haruna *et al.* (2006), who found that NAD(P)H oxidase and uncoupled edothelial NO synthase were responsible for the increased vascular oxidative stress and consequently for endothelial dysfunction in AA. Improvement of aortic endothelial function induced by SO administra-

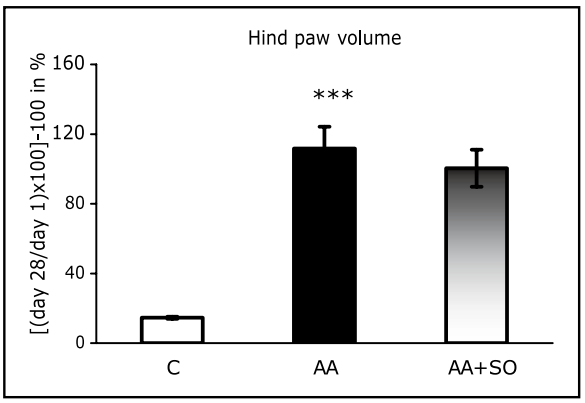

Fig. 1: Hind paw volume measured on day 28 of adjuvant arthritis in control rats (C), rats with adjuvant arthritis (AA), and rats with adjuvant arthritis treated with sesame oil (AA+SO). Data are expressed as HPV [(day 28 / day 1).100]-100 in percentages. Values are means ± SEM of n=8.***P < 0.001 AA *versus* C.

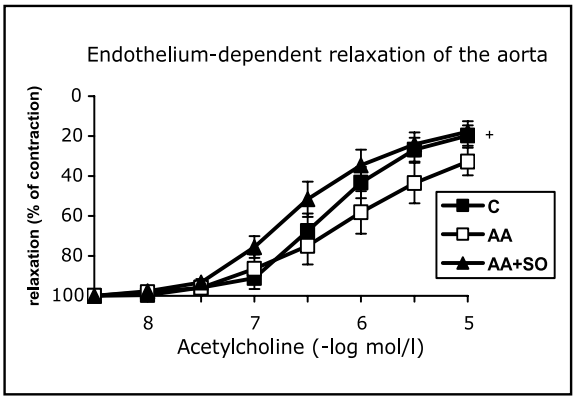

Fig. 2: Responses to acetylcholine of the phenylephrine precontracted aorta of control rats (C ■), rats with adjuvant arthritis (AA □), and rats with adjuvant arthritis treated with sesame oil (AA+SO▲). Values are means ± SEM of n=8. *$p < 0.05$ AA+SO *versus* AA.

tion, found in our experiments, is further evidence of the participation of oxidative stress in AA and simultaneously of antioxidant properties of SO.

CONCLUSIONS

Sesame oil has beneficial effects on oxidative stress induced biochemical changes occurring in adjuvant arthritis, moreover it improves endothelium-dependent relaxation of the aorta and tends to decrease hind paw edema. Our results suggest that oral administration of sesame oil could contribute to the treatment of rheumatoid arthritis, as well as other diseases with oxidative stress involved in their pathogenesis.

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