

Anti-Inflammatory Effects of Thyme Essential Oil in Mice

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Abstract

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Plant essential oils are plant secondary metabolites possessing various pharmacological properties, primarily anti-oxidative, antimicrobial or immunomodulatory ones. The aim of this work was to study the effects of thyme essential oil dietary administration in murine DTH/CHS reaction, carrageenan paw oedema and TNBS colitis. Thyme essential oil was added to the murine diet at three concentrations (5000, 2500 and 1250 ppm) and fed to Balb/c mice. The extent of ear swelling in DTH/CHS reaction and paw oedema induced by carrageenan application was measured using the Mitutoyo thickness gauge. In the model of TNBS colitis we evaluated the changes in body weight, the colon weight : body weight ratio, bacterial translocation to mesenteric lymph nodes, and macroscopical and histological scores. IL-1 β and IL-6 messenger RNA expression in colonic samples of one experimental group were assessed using quantitative real-time reverse transcriptase PCR. Dietary supplementation with 5000 ppm of thyme essential oil significantly decreased paw oedema and ear swelling. This thyme essential oil concentration caused a significant inhibition of total mRNA IL-1 β expression in the mouse colon, and markedly decreased the macroscopic and microscopic scores of colitis. On the other hand, the 1250 ppm of thyme essential oil in diet increased ear oedema induced by oxazolone application in mice. Our study indicates that thyme essential oil is able to affect murine experimental inflammatory models depending on the concentration used. It is concluded that the anti-inflammatory effects of thyme essential oil should be interpreted with a caution due to its contradictory, dose-related effects.

Inflammation, DTH/CHS reaction, carrageenan paw oedema, colitis, thyme essential oil, cytokines

A large number of plant species contain various bioactive compounds exhibiting health-beneficial properties, anti-oxidative, anti-inflammatory and mainly antimicrobial effects, and their preventive and therapeutic use increases. Numerous natural products have been already tested in various animal models for the development of new anti-inflammatory therapeutics.

Contact hypersensitivity (CHS) experimental models are commonly used in rodents to investigate possible anti-inflammatory agents (Verdrengh et al. 2003; Wee et al. 2005; Puebla-Pérez et al. 2003). CHS is one of the forms of delayed type of hypersensitivity (DTH) which is a T-cell-mediated, antigen-specific skin inflammation induced by skin exposure to hapten (e.g. oxazolone, dinitrofluorobenzene). Carrageenan-induced mouse paw oedema is frequently used to determine the anti-inflammatory activity of various bioactive compounds. Recently Posadas et al. (2004) divided the inflammatory response to carrageenan into an early phase lasting 6 h and a second late response that peaks at 72 h, although only 7- or 8-week old mice displayed a consistent response in both phases. Carrageenan-induced mouse paw oedema has been used for assessment of the anti-inflammatory activity of many plant extracts and essential oils (Khalil et al. 2006; Orhan et al. 2006; Hajhashemi et al. 2003).

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Experimental colitis in mice and rats induced by the administration of various chemical agents is widely used to study various compounds as possible therapeutic agents for inflammatory bowel disease (IBD). Pérez-Navarro et al. (2005) studied 4 models of acute and 5 models of chronic colonic inflammation. The administration of TNBS (2, 4, 6-trinitrobenzenesulphonic acid) in 50% ethanol resulted in chronic inflammations of the colon, and produced severe necrotic lesions that healed after several weeks, leaving scars and fibrosis as sequelae. Moreover the IFN- γ levels were significantly increased in the TNBS model in comparison with other acute and chronic models. Animal models of colitis have been employed to assess the anti-inflammatory effects of plant extracts or their components, polyherbal formulation and probiotics (Jagtap et al. 2004; Mahgoub 2003; Osman et al. 2006).

The anti-inflammatory actions of thyme extracts and their components have been evaluated only in a few *in vivo* and *in vitro* studies. Extract from *Thymus vulgaris* significantly inhibited inducible nitric oxide synthase mRNA expression (Vigo et al. 2004). P-cymene, thymol, carvacrol and γ -terpinene as major constituents of the essential oil of thyme species have been identified as effective antibacterials in *in vitro* studies (Burt 2004). So far there has been no available study on the effects of thyme extracts on the gastrointestinal system. Our aim therefore was to examine whether dietary addition of thyme essential oil could have positive effects in experimental intestinal inflammation induced by TNBS administration in mice, and to compare its effects in two other established anti-inflammatory murine models - the delayed-type hypersensitivity reaction to oxazolone and carrageenan paw oedema.

Materials and Methods

Animals and treatment

Seven-week-old male Balb/c mice weighing 17–23 g were purchased from Velaz (Prague, Czech Republic). After a period of adaptation, weight-matched animals were randomized into groups. All animal experimentation was reviewed and approved by the Ethics Committee of the Institute of Animal Physiology.

Thyme aromatic oil (Thymi aetheroleum - Ph.Eur. 4) purchased from Calendula, a.s. (Nová Lúbovňa, Slovakia; lot 5-015-003-10-04) containing approx. 48% of p-cymene and 24% of thymol was added to powdery commercial rodent diet (Diet for laboratory mice and rats SPF, M1; František Machal, Ricmanice, Czech Republic) in 1% edible soy oil (Brölio, Germany) at the following concentrations: 1250 ppm (wt/wt) - group A; 2500 ppm (wt/wt) - group B; 5000 ppm (wt/wt) - group C. The diet for control and sham groups was prepared similarly using only 1% edible soy oil. The diets were fed *ad libitum* during all experiments starting 7 days before administration of TNBS enema and 5 days before hypersensitisation in the DTH/CHS model or the application of carrageenan in the paw oedema model.

Induction of DTH/CHS reaction

The DTH reaction was induced in 7-week-old male Balb/c (group A, B - n = 12; group C - n = 13; group control K - n = 14) mice as previously described (Lange-Asschenfeldt et al. 2002). The mice were sensitised by topical application of a 2% oxazolone (SIGMA, Steinheim, Germany) solution in acetone/olive oil (4 : 1 vol/vol) onto the shaved abdomen (50 μ l) and onto each paw (5 μ l). Five days after sensitisation, the right ears were challenged by topical application of 10 μ l of a 1% oxazolone solution, whereas the left ears were treated with vehicle alone. Ear thickness was measured before hypersensitisation, and 24, 48 h after topical application of 1% oxazolone, using a Mitutoyo thickness gauge (Mitutoyo, No. 7313, Japan). The increase in ear thickness was calculated as the difference between the right ear volume (oxazolone) and the left ear volume (vehicle) measured at each time point.

Carrageenan paw oedema

Seven-week-old male Balb/c mice were divided into groups (n = 12 each group) and anaesthetized with ketamine-xylazine (32 mg/kg - 2.3 mg/kg; i.p.). Each group of animals received subplantar administration of 50 μ l of saline to the left paw or 50 μ l of carrageenan 1% (w/v) (SIGMA, Steinheim, Germany) in saline to the right paw. The paw width was measured with a Mitutoyo thickness gauge (Mitutoyo, No. 7313, Japan) immediately before subplantar injection, and 2, 4, 24 h thereafter. The increase in paw volume was calculated as the difference between the right paw volume (carrageenan) and the left paw volume (saline) measured at each time point.

Induction of TNBS colitis

Mice were anaesthetized with ketamine-xylazine (32 mg/kg - 2.3 mg/kg; i.p.) and colitis was induced by intrarectal administration of 120 mg/kg of the hapten reagent TNBS (Fluka, Steinheim, Germany) in 50% ethanol,

and they were then kept in a vertical position for 30 seconds. The sham group received 50% ethanol alone through the same technique. The total injection volume was 30 μ l. Development of colitis was assessed daily by measurement of body weight. The mortality rate was observed during the study. The mice were killed by cervical dislocation 5 days after TNBS administration. Their abdomens were soaked with 70% ethanol and an incision was made through the skin and peritoneum by using sterile scissors. The abdominal wall was reflected, exposing the peritoneal cavity. The mesenteric lymph node draining the caecum and colon was excised with another set of sterile instruments for the determination of bacterial translocation. Afterwards the colons were removed, opened longitudinally and cleared of faecal material with a gentle spray of 0.9% saline solution. The extent of mucosal damage was assessed using the colon macroscopic scoring system (Bukovská et al. 2007; adapted from Wallace et al. 1989).

Ulceration: 1 - focal hyperemia, no ulcer; 2 - ulceration, no hyperemia/bowel wall thickening; 3 - ulceration, inflammation at one site; 4 - ulceration, inflammation at 2 or more sites; 5 - major injury > 1cm; 6 - 10 major damage > 2 cm.

Adhesion: 1 - minor (colon easily separated from other tissue); 2 - major.

Diarrhoea: 1.

Bowel wall thickening: 1.

After scoring, the detached colon was dried and weighed. The colon weight/body weight ratio was calculated as a marker of colonic inflammation. Immediately after weighing, the macroscopically most intensively affected segment was cut for microscopic examination and assessment of IL-1 β and IL-6 messenger RNA expression.

Histopathological assessment of colonic damage

The colons of 8 mice from each group underwent microscopic examination. For histological evaluation, colon tissues (ca 5 mm \times 5 mm) were fixed in 4% formalin in 0.1 M phosphate buffer, dehydrated with increasing concentrations of ethanol, embedded in paraffin, and sectioned. Sections (7 μ m thick) were mounted on slides, cleared, hydrated and stained with haematoxylin and eosin. The slides were examined with a microscope (BX51 Olympus, Japan) and digital photographs were taken. Histological changes were classified according to Ameho's score: 0 Histological findings identical to normal rats; 1 Mild mucosal and/or submucosal inflammatory infiltrate (admixture of neutrophils) and oedema. Punctate mucosal erosions often associated with capillary proliferation. Muscularis mucosae intact; 2 Grade 1 changes involving 50% of the specimen. 3 Prominent inflammatory infiltrate and oedema (neutrophils usually predominating) frequently with deeper areas of ulceration extending through the muscularis mucosae into the submucosa. Rare inflammatory cells invading the muscularis propriae but without muscle necrosis; 4 Grade 3 changes involving 50% of the specimen; 5 Extensive ulceration with coagulative necrosis bordered inferiorly by numerous neutrophils and lesser numbers of mononuclear cells. Necrosis extends deeply into the muscularis propria; 6 Grade 5 changes involving 50% of the specimen (Ameho et al. 1997).

Bacterial translocation

The mesenteric lymphatic nodules were removed, weighed separately and placed in a sterile grinding tube. The samples were homogenized with 1000 μ l of PBS. After mechanical grinding, 100 μ l aliquots were placed onto Mc agar plates (Imuna, Šarišské Michaľany, Slovakia). All agar plates were incubated aerobically for 24 h at 37 $^{\circ}$ C. Quantitative culture results were determined as the logarithm of the number of colony-forming units (cfu) per 0.01 g of tissue, calculated with the following formula: number of cfu \times reciprocal of dilution \times 10/weight of tissue.

Real-time reverse transcriptase - PCR quantification of cytokine mRNA

Quantification of IL-1 β and IL6 mRNA was carried out as described in Bukovská et al. (2007). Briefly, total RNA was isolated from mouse colon tissue with Trizol Reagent (Invitrogen Life Technologies, Karlsruhe, Germany), cleaned and DNase I treated with RNeasy Micro kit (Qiagen, Hilden, Germany). Complementary DNA (cDNA) was then prepared using Superscript II Transcriptase (Invitrogen Life Technologies). The pool of mouse colon RNA gained from aliquots of all samples served as a standard RNA. Relative standard curves were generated by real-time PCR system Mx 3000P (Stratagene, La Jolla, CA) amplifying target sequences in cDNAs prepared from serial dilutions of the standard RNA. PCR reactions were carried out in duplicates using oligonucleotide primers specific for IL-1 β (interleukin 1 beta), IL-6 (interleukin 6), and HPRT (hypoxanthine guanine phosphoribosyl transferase 1), as described in Bukovská et al. (2007). The IL-1 β and IL6 quantities were normalized to the quantity of HPRT or to the total RNA quantity.

Statistical analysis

The results are expressed as mean \pm SD. Student's *t*-test was used for differences in ear thickness and paw width. Mann-Whitney U test was used for macroscopic damage scores, microscopic damage scores, bacterial translocation to mesenteric lymph nodes and cytokine mRNA expression. Chi-square test was used to detect differences in mortality rates. Student's *t*-test was used for the colon weight: body weight ratio. Values of *P* < 0.05 were considered as significant.

Results

DTH/CHS reaction

The consumption of diets containing thyme essential oil (TEO) induced dose-dependent

Table 1. Effects of thyme essential oil dietary administration on a) DTH/CHS reaction in mice; b) carrageenan-induced paw oedema in mice (swelling thickness $\times 10^{-2}$ mm)

a) DTH/CHS			
	n	24 h	48 h
Control	14	35.5 \pm 8.3	15.2 \pm 4.8
TEO 1250	12	41.8 \pm 5.4*	22.0 \pm 5.3**
TEO 2500	12	37.8 \pm 5.0	18.8 \pm 3.4*
TEO 5000	13	30.9 \pm 3.9*	13.8 \pm 3.6

b) Carrageenan-induced paw oedema				
	n	2 h	4 h	24 h
Control	12	43.7 \pm 9.5	36.8 \pm 7.9	55.3 \pm 9.3
TEO 1250	12	46.7 \pm 14.0	39.1 \pm 9.9	50.3 \pm 10.1
TEO 2500	12	42.8 \pm 12.4	31.6 \pm 13.9	44.4 \pm 7.4**
TEO 5000	12	34.2 \pm 13.7*	25.9 \pm 9.1**	39.9 \pm 10.8**

Values are arithmetical means \pm SD. TEO 1250 - 1250 ppm thyme essential oil in diet; TEO 2500 - 2500 ppm thyme essential oil in diet; TEO 5000 - 5000 ppm thyme essential oil in diet. Statistical differences between control and experimental groups (Student's *t*-test): * $P \leq 0.05$, ** $P \leq 0.01$

oedema formation in mice fed the diet with 5000 ppm TEO and in control mice ($P < 0.05$), while the consumption of the diet with 1250 ppm TEO increased paw inflammation compared to the control group, but the changes were non-significant (Table 1b). Similar dose-dependent changes of paw oedema in animals fed the TEO diet were also observed at later measurement points. Both measurements (4 and 24 h) showed significant differences between oedema formation in mice treated with the 5000 ppm TEO diet and in control mice ($P < 0.01$). A similar decrease of paw swelling was observed in mice fed with the 2500 ppm TEO diet 24 h after carrageenan application ($P < 0.01$). Paw oedema of mice on the 1250 ppm TEO diet was decreased in comparison to the control group (24 h interval), but the changes were non-significant due to high variability of this experimental model.

TNBS induced colitis

Our results show that the macroscopic/microscopic damage scores and colon weight/body weight ratio of mice in the sham group were highly significantly lower than those of mice in

Table 2. Effects of thyme essential oil dietary administration on TNBS-induced colitis in mice - mortality, body weight changes, macroscopic and microscopic scores, colon weight /body weight ratio, bacterial translocation

	Sham	TNBS	TEO 1250	TEO 2500	TEO 5000	
Number of treated mice	12	15	16	16	16	
Number of surviving mice	12	12	15	15	13	
Mortality (%)	0	20	6.25	6.25	18.8	
Relative weight on day 5 (%)	103.86 \pm 2.09***	80.11 \pm 9.83	84.85 \pm 12.68	80.82 \pm 12.94	87.94 \pm 14.87	
Macroscopic score	0.08 \pm 0.29***	6.58 \pm 4.66	5.33 \pm 3.94	6.67 \pm 5.05	3.46 \pm 4.20*	KW: ***
Microscopic score	0 \pm 0***	4.38 \pm 1.77	3.25 \pm 2.19	3.75 \pm 2.32	1.88 \pm 2.59*	KW: ***
Colon weight (% of b.w.)	1.56 \pm 0.12***	2.47 \pm 0.53	2.26 \pm 0.38	2.36 \pm 0.62	2.2 \pm 0.57	
Bacterial translocation	0 \pm 0**	2.61 \pm 2.12	2.18 \pm 1.86	2.56 \pm 1.48	2.13 \pm 1.61	KW: ***

Values are arithmetical means \pm SD. Statistical differences between untreated colitic animals and other groups of animals (weight *t*-test; translocation and scores Mann-Whitney test): * $P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$; KW - Kruskal-Wallis test; Sham - control animals; TNBS - untreated colitic animals; TEO 1250 - colitic animals on 1250 ppm thyme essential oil in diet; TEO 2500 - colitic animals on 2500 ppm thyme essential oil in diet; TEO 5000 - colitic animals on 5000 ppm thyme essential oil in diet.

changes of DTH reactions in mice. After 24 h significant differences were observed between ear swelling of mice on 5000 ppm and 1250 ppm TEO in diet ($P < 0.05$). The diet with 5000 ppm TEO decreased ear inflammations in the mice, while 1250 ppm TEO diet produced augmentation of ear swellings (Table 1a). The next measurement 48 h after challenge showed significantly increased ear swelling in animals on 1250 ppm ($P < 0.01$) and 2500 ppm ($P < 0.05$) TEO in diet. Dietary supplementation with 5000 ppm TEO decreased ear inflammations, but the changes were not significant.

Mouse paw oedema

As early as the first measurements, 2 h after induction of paw oedema, dose-dependent changes of reaction in thyme essential oil experimental groups were indicated. Significant difference was observed between

the TNBS group ($P < 0.001$) (Table 2). Colon weight/body weight ratio and macroscopic/microscopic damage scores in mice on 2500 ppm TEO in diet were comparable with mice in the TNBS group. The 1250 ppm TEO diet decreased the colon weight/body weight ratio and macroscopic/microscopic damage scores compared with mice in the TNBS group, but the changes were not significant (Table 2). In contrast to this, we observed that 5000 ppm TEO diet significantly decreased the total macroscopic/microscopic damage scores of mice compared to the TNBS group ($P < 0.05$) (Table 2), as well as the colon weight/body weight ratio in this group ($P > 0.05$).

Sham mice receiving only 50% ethanol intrarectally showed a significant reduction of bacterial translocation to mesenteric lymph nodes in comparison with TNBS-treated mice ($P < 0.05$, Table 2). However, dietary application of all tested concentrations of TEO did not significantly decrease bacterial translocation to lymph nodes.

Morphological markers of the group with 5000 ppm TEO in diet indicated a decrease in the degree of colonic inflammation, so mRNA expressions of selected cytokines (IL-1 β and IL-6) were analyzed in this group and compared with the TNBS control. Quantities of cytokines were standardized to the HPRT expression (the most stably expressed housekeeping gene evaluated by geNorm software) and to the input of total RNA into RT-PCR. Our results indicate a decrease in cytokine concentrations in mice on 5000 ppm TEO in diet, though we only detected significant changes in IL-1 β mRNA expression normalized to total RNA ($P < 0.05$, Table 3).

Table 3. Effects of 5000 ppm thyme essential oil dietary administration on TNBS-induced colitis in mice: IL-1 β and IL-6 mRNA expression

	TNBS	TEO 5000	Mann-Whitney test
IL-1 β /RNA	746.7 \pm 1081.9	149.3 \pm 237.6	*
IL-1 β /HPRT	1.5 \pm 1.50	0.42 \pm 0.645	NS
IL-6/RNA	733.1 \pm 587.5	237.5 \pm 302.6	NS ($P = 0.064$)
IL-6/HPRT	0.80 \pm 0.65	0.31 \pm 0.43	NS

Values are arithmetical means \pm SD; number of samples (animals) in each group was 6 - 8. Statistical differences between (TNBS) untreated colitic animals and (TEO 5000) colitic animals on 5000 ppm thyme essential oil in diet.

(Mann-Whitney test): * $P \leq 0.05$, NS $P > 0.05$

Discussion

We evaluated the effects of thyme essential oil dietary administration in mice using three different animal models. Our results indicate that immune reactions caused by oxazolone and carrageenan application could be modulated by thyme essential oil depending on the concentrations used. High concentration (5000 ppm) of

TEO attenuated the DTH/CHS reaction to oxazolone as well as carrageenan paw oedema in Balb/c mice. On the other hand, two lower concentrations tested (2500 ppm and 1250 ppm of TEO) enhanced the murine DTH/CHS reaction. This observation could be correlated with the known immunomodulatory effects of carvacrol, one of the main substances in thyme essential oil. Carvacrol selectively activates the ERK (Extracellularly-Responsive Kinase) subgroup in Jurkat T-cells and stimulates the JNK (c-Jun N-terminal Kinase) subgroup in THP-1 monocytic cells (Human acute monocytic leukaemia cell line), and so may act as an effective agent to modulate the functions of immuno-responsive cells via intracellular signalling pathways (Chan et al. 2005). Very recently Elhabazi et al. (2006) have shown that thyme extracts increase the number of polymorphonuclears, total lymphocytes, T CD4⁺, CD8⁺ and NK cells. Similarly, "Oregpig" (commercial feed additive containing 60 g carvacrol and 55 g thymol per kilogram) had non-specific immunostimulatory effects on porcine immune cells, and the proportion of CD4, CD8, MHC class II antigen, and non-T/non-B cells in peripheral blood lymphocytes was significantly higher in the Oregpig-receiving pigs than in the control animals (Walter and Bilkei 2004). On the other hand, Aydin et al. (2005) showed in their *in vitro* study that high concentrations of carvacrol, thymol and γ -terpinene are able to induce lymphocytes DNA damage. This fact could

partly explain the significant anti-inflammatory effect of the highest (5000 ppm) TEO dose in DTH/CHS reaction and paw oedema.

In carrageenan paw oedema there was a dose-dependent effect of TEO in diet comparable to DTH reaction, but we did not detect any significant immunostimulatory effect at low concentrations. The observed anti-inflammatory effects of thyme essential oil could be correlated with its *in vitro* ability to manipulate neutrophil activation (Abe et al. 2003). Furthermore, thyme essential oil shows anti-oxidant activity and has an inhibitory effect on lipid peroxidation, which could decrease the strength of inflammatory response in carrageenan paw oedema (Bozin et al. 2006).

TNBS-induced colitis is one of the models of intestinal inflammation resembling Crohn's disease. The dietary administration of 5000 ppm of TEO significantly improved the analyzed indicators of TNBS-induced colitis. This fact may be attributed to the above-mentioned anti-oxidative and anti-inflammatory activities of thyme essential oil, which are complemented by the antiseptic properties of thyme oil and its constituents (Jugl-Chizzola et al. 2005; Burt 2004). Antibacterial effects of thyme essential oil may influence intestinal microflora, thus helping to protect TNBS-affected areas of colonic mucosa; however, we did not detect any significant changes in bacterial translocation to lymph nodes. The protective effect of the high concentration of thyme essential oil on intestinal mucosa was also indicated by a reduced IL-1 β /RNA ratio, similar to the positive impact of an oregano and thyme essential oil dietary combination on local cytokine levels in TNBS-induced colitis (Bukovská et al. 2007).

Our study indicates that thyme essential oil dietary application is able to affect murine experimental inflammatory models depending on the concentration used. High concentration of thyme essential oil in all models has anti-inflammatory effects, but low concentration leads to an enhanced reaction in DTH/CHS. Evidently, it is necessary to study in greater detail the immunomodulatory properties of thyme extracts. It could be concluded that the anti-inflammatory effects of thyme essential oil should be interpreted with caution, due to its contradictory dose-related effects.

Protizápalové účinky tymianového éterického oleja u myší

Rastlinné éterické oleje patria medzi sekundárne metabolity rastlín s rozličnými farmakologickými vlastnosťami, predovšetkým antioxidačnými, antimikrobiálnymi, imunomodulačnými. Na druhej strane môžu éterické oleje spôsobiť alergické reakcie alebo mať toxický vplyv na živé organizmy. Cieľom tejto práce bolo štúdium vplyvu tymianového éterického oleja na tri myšacie štandardizované modely (DTH/CHS, opuch labiek indukovaný karagenanom, TNBS kolitída). Tymianový éterický olej bol pridávaný do krmiva Balb/c myšiam v troch koncentráciách (5000, 2500 a 1250 ppm). Rozsah zdurenia ušnic v DTH/CHS reakcii a opuch labiek indukovaný aplikáciou karagenanu bol meraný pomocou hrúbkomeru (Mitutoyo). V modeli TNBS kolitídy sme hodnotili zmenu telesnej hmotnosti myší, pomer hmotností kolónov a telesnej hmotnosti myší, bakteriálnu translokáciu do mezenterálnych lymfatických uzlín, makroskopické a histologické skóre. V skupine s najvyššou koncentráciou tymianového éterického oleja bola pomocou kvantitatívnej RT-PCR v reálnom čase stanovená aj expresia mRNA IL-1 β a IL-6 v tkanive hrubého čreva. Suplementácia krmiva tymianovým éterickým olejom v dávke 5000 ppm signifikantne znížila edém labiek ako aj zdurenie ušnic u myší. Táto koncentrácia éterického oleja takisto spôsobila signifikantnú inhibíciu expresie celkovej mRNA IL-1 β v tkanive hrubého čreva myší, pričom významne znížila makroskopické aj mikroskopické skóre kolitídy. Na druhej strane podávanie tymianového éterického oleja v najnižšej dávke (1250 ppm) spôsobilo zosilnenie opuchu uší po aplikácii oxazolónu. Naše experimenty svedčia o tom, že tymianový éterický olej môže ovplyvniť myšacie zápalové modely v závislosti na použitej koncentrácii. Dosiahnuté výsledky naznačujú, že protizápalové účinky tymianového

éterického oleja je potrebné interpretovať opatrne vzhľadom na jeho protichodné účinky v závislosti na použitej dávke.

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