Phytomedicine 17 (2010) 707–713

Contents lists available at ScienceDirect

Phytomedicine

journal homepage: www.elsevier.de/phymed

Antiasthmatic effect of *Nigella sativa* in airways of asthmatic patients

M.H. Boskabady *, N. Mohsenpoor, L. Takaloo

Department of Physiology, Medical School and Pharmacology Research Centre, Mashhad University of Medical Sciences, Mashhad, Iran

ARTICLE INFO

Keywords:
Asthma
Antiasthmatic effect
Nigella sativa
Airways

ABSTRACT

In the present study, the antiasthmatic (bronchodilatory) effect of the boiled extract of *Nigella sativa* in the airways of asthmatic patients was examined.

The bronchodilatory effects of 50 and 100 mg/kg of boiled extract in comparison with 6 mg/kg theophylline were studied on 15 asthmatic patients. Pulmonary function tests (PFTs) including forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), maximal mid expiratory flow (MMEF), maximal expiratory flow at 75, 50 and 25% of the FVC (MEF_{75}, MEF_{50}, and MEF_{25}, respectively) and specific airway conductance (sGaw) were measured before administration and repeated , 30, 60, 90 120, 150, and 180 min after administration of the oral extract and theophylline.

The results showed that the extract caused significant increases in all measured pulmonary function tests (PFTs), in most time intervals, ($p < 0.05$ to $p < 0.001$). However, the increase in FEV_1, MMEF and MEF_{50} due to both doses of boiled extract and increase in MEF_{75} and MEF_{25} due to its lower doses were significantly lower than those of theophylline ($p < 0.05$ to $p < 0.001$). The onset of brochodilatory effect of extract was similar to that of theophylline beginning 30 min, and the effect of extract decline after 150 min following administration similar to the effect of theophylline. The effect of both doses of the extract was also significantly less than that of salbutamol at 30 minutes post administration ($p < 0.001$ for all cases).

The results of the present study showed that *Nigella sativa* has a relatively potent antiasthmatic effect on asthmatic airways. However, the effects of boiled extract of this plant on most measured PFTs was less than those of theophylline at concentrations used.

Introduction

Several therapeutic effects including the effect on asthma and dyspnea have been described for the seeds of *Nigella sativa* in Iranian ancient medical books (Ave-Sina, 1990). The relaxant effects of this plant on different smooth muscle preparations including rabbit aorta (Aqel, 1992), rabbit jejunum (Aqel, 1993), and guinea pig isolated tracheal muscle (Reiter and Brandt, 1985) were shown. It was shown the volatile oil from *Nigella sativa* protected guinea pigs against histamine-induced bronchospasm, but it did not affect histamine H_1 receptors in isolated tissues (Mahfouz and El-Dakhakhny, 1960). However, increasing respiratory rate and intratracheal pressure of guinea pigs due to i.v. administration of volatile oil from *Nigella sativa* has been demonstrated (El-Tahir et al., 1993).

The results of our studies also showed different pharmacological effects of *Nigella sativa* on guinea pig tracheal chains including: relaxant and functional antagonistic effects on muscarinic receptors (Boskabady and Shahabi, 1997), inhibitory effect on histamine (H_1) receptors (Boskabady and Shiravi, 2002) inhibitory effect on calcium channels (Boskabady and Shirmohammadi, 2002), opening effect on potassium channels (Boskabady et al., 2004c), stimulatory effect on β- adrenoceptors (Boskabady et al., 2004b). The antitussive effect of this plant on the guinea pig (Boskabady et al., 2004a) was also demonstrated.

Therefore, in the present study, the antiasthmatic effect of boiled extract from *Nigella sativa* on asthmatic airways was examined.

Materials and Methods

Plant, extract and drugs

Nigella sativa was collected from Torbat Heydarieh (north east Iran), and dried at room temperature in the absence of sunlight. The plant was identified by botanists in the herbarium of Ferdowsi University of Mashhad; and the specimen number of the plant is 293-0303-1. The boiled extract of the plant was prepared as follows: Twenty grams of the chopped, dried seeds of the plant was boiled with 100 ml distilled water for 15 minutes

* Corresponding author. Tel.: +98 511 8828565; fax: +98 511 8828564.
E-mail addresses: boskabadymh@mums.ac.ir, mhboskabady@hotmail.com (M.H. Boskabady).

0944-7113/$ - see front matter © 2010 Elsevier GmbH. All rights reserved.
doi:10.1016/j.phymed.2010.01.002

and allowed to cool at room temperature. The extract was then filtered with a clean cotton cloth and the volume of extract adjusted to 100 ml by adding saline solution. Therefore the final extract concentration was 200 mg/ml.

Theophylline syrup (Razak Company, Iran)

Characterization of boiled extract of Nigella sativa by HPLC

The quality of boiled extract of *Nigella sativa* was characterized by HPLC (Waters 474, Waters Corporation, MA, USA) finger print. The extract was dissolved in distilled water:methanol mixture (50:50) and then filtered through 0.22 μm membrane filter. 20 μl of sample (5 mg/ml) was injected to the reverse phase HPLC column (C18). The mobile phase was consisted of water: methanol: 2-propanol (50:45:5) with an isocratic elution at the flow rate of 1 ml/minute. The peaks were monitored at 440 nm (Fig. 1).

Studied population

Fifteen asthmatic patients (mean age ± SD; 42.80 ± 11.42, 5M, 10F) were recruited from the Asthma Clinic, Ghaem Medical Centre, Mashhad University of Medical Sciences (Table 1). All patients had the following criteria: 1) previously diagnosed asthma by a physician and having two or more of the following symptoms: recurrent wheeze, recurrent cough or chest tightness at rest; wheeze, cough or tightness during night or early morning; wheeze or cough during exercise, 2) having FEV_1 and/or PEF less than 80% predicted values, 3) at least 15% increase in FEV_1 and/or PEF due to 200 μg salbutamol inhalation 4) had no history or symptoms of cardiovascular or other respiratory diseases that required treatment (excluding the common cold). The studied patients had moderate to severe asthma according to the Gina guideline (Shefer, 2002) and all were on active treatment that included inhaled beclomethasone dipropianate (600-1600 μg) or fluticasone propionate (500 μg). Patients with cold or other respiratory or heart diseases were excluded from the study. The protocol was approved by the Ethics Committee of our institution, and each subject gave an informed consent. The study was carried out during spring and summer 2006 in the Department of Physiology and Pharmacological Research Canter of Medical Plants, Mashha University of Medical Sciences.

Protocol

Each subject attended the laboratory on four occasions, with at least 48 hours between attendances over a period not exceeding 2 weeks. The study was performed at approximately the same time of day on each occasion (Heaton et al., 1988). Subjects refrained from caffeinated drinks for 2 hours before challenge and from using bronchodilator inhalers for at least 8 hours, and from theophylline for 12 hours: but other asthma medications were allowed to be taken regularly according to standardized schedule prior to different attendances. In random order and in double blind and cross over manner, on the four days the following drugs were administered: 1) Oral theophylline (syrup, 6 mg/kg), 2) Oral boiled extract of *Nigella sativa* (50 mg/kg) and 3) Oral boiled extract of *Nigella sativa* (100 mg/kg) and 4) 200 μg inhaled salbutamol.

Table 1
Characteristics of asthmatic subjects included in the study.

Subjects	Sex &Age	Height(cm)	Smoking	Treatments
1	M-65	168	–	Atr-Sal-The-Bec
2	F-33	158	–	Bec-Sal-The-Pr
3	F-39	176	–	Sal-The-Pr- FL
4	M-39	165	–	Bec- Sal-The-Pr
5	M-23	167	–	Sal-The-Pr-Fl
6	M-57	162	–	Bec-Pr-The-Sal
7	F-47	155	–	Bec-Sal-The-Pr
8	F-42	160	–	The-Sal-Bec
9	F-47	167	–	Bec-Sal-The-Pr
10	F-23	166	–	Bec- Sal-The-Pr
11	F-48	159	–	The-Sal-Bec
12	F-40	157	–	The-Sal-Bec
13	F-39	163	–	The-Sal-FL
14	M-54	175	–	The-Sal -FL
15	F-46	158	–	The-Sal-Pr
Mean	42.80	163.80		
SD	11.42	6.27		

Abbreviations; Bec: Beclomethasone propionate; Pr: Prednisolone; The: Theophylline; Sal: Salbutamol inhaler; Atr:Atrovent; FL: Fluticasone propionate.

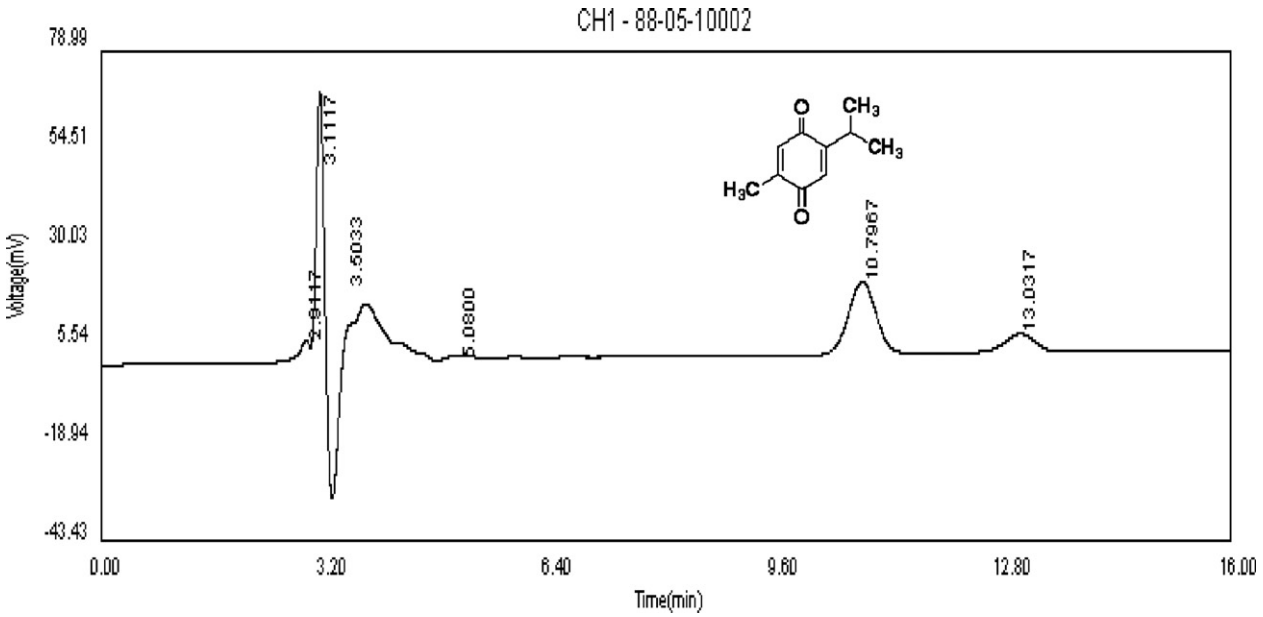

Fig. 1. HPLC fingerprint of the boiled extract of *Nigella sativa* (500 mcg/ml) illustrating thymoquinone ($C_{10}H_{12}O_2$, R_T 10.797).

Forced expiratory volume in one second (FEV_1), peak expiratory flow (PEF), maximal mid expiratory flow (MMEF), maximal expiratory flow at 75, 50 and 25% of the FVC (MEF_{75}, MEF_{50}, and $MEF_{25,}$ respectively) and specific airway conductance (sGaw) were measured using body plethysmograph (200 Autobox DL, 2130 spirometer, Sensormedics, USA) before and at different time intervals after drug administration (30, 60, 90, 120, 150 and 180 mins). In the occasion of salbutamol administration, PFT were measured only before and at 30 mins after drug administration. Pulmonary function testing was performed by a trained final year medical student using the acceptability standards outlined by the American Thoracic Society (American Thoracic Society, 1995) with subjects in a standing position and wearing nose clips. Prior to pulmonary function testing, the required manoeuvre was demonstrated by the operator, and subjects were encouraged and supervised throughout test performance.

The increase in measured pulmonary function tests (PFT) after oral theophylline and extract from *Nigella sativa* (in percentage) was calculated as follows:

$$\frac{\text{PFT values after drug administration} - \text{baseline PFTs}}{\text{Baseline PFTs}} \times 100$$

Data analysis

Based on the prevalence of asthma in Iran, using the PPS sampling method, it was calculated that a minimum of 15 subjects would be needed to detect a 4% difference with an α error of 1% and a power of 95%. The data of increase in measured PFTs and their baseline were expressed as mean ± SEM, but those of age and height were expressed as mean ± SD. The increase in measured PFTs in different time intervals after drugs administration was compared with those of baseline values using rpeated measurement analysis of variance (ANOVA) with Tukey post test. The increase in measured PFTs due to Theophylline and two doses of extract and baseline PFT values in three attendances were compared using Kruskal Wallis test. The increase in measured PFTs due to inhaled salbutamol and two doses of extract and baseline PFT values in four attendances were compared using Kruskal Wallis test. Significance was accepted at $p < 0.05$.

Results

Characterization of boiled extract

Thymoquinone of the extract from *Nigella sativa* was identified using HPLC method in the Dept. of Pharmacology, Medical School, Mashhad university of Medical Sciences (Fig. 1).

Baseline PFT values

Most measured PFT values were abnormally low (lower than 80% predicted values) in all studied patients. In addition there were no significant differences in baseline PFTs among attendances (Table 2).

The effect of salbutamol on PFT values

All PFT values increased more than 12%, 30 min after administration of 200 μg inhaled salbutamol and two doses of the extract (Fig. 2). The effect of both doses of the extract was significantly less than that of salbutamol at 30 minutes post administration ($p < 0.001$ for all cases, Fig. 2).

Antiasthmatic effect of theophylline and the extract

Theophylline syrup caused a significant increase in all measured PFT values ($p < 0.05$ to $p < 0.001$) (Table 3). Significant increase in PFTs due to high dose of boiled extract from *Nigella sativa,* occurred 30 min after administration (except MEF_{75}) and was maintained until 150 min post administration ($p < 0.05$ to $p < 0.001$) (Table 4). The increase in measured PFTs after treatment with lower dose of boiled extract of *Nigella sativa* became statistically significant, mainly 30 min after administration ($p < 0.05$ to $p < 0.01$) (Table 5).

The antiasthmatic effect of theophylline syrup began at 30 min and started to decline 150 min after administration (Table 3, Fig. 3). The effect of boiled extract from *Nigella sativa* on PFTs began 30 min after administration and declined after 150 min (Table 4 and 5, Fig. 3).

Comparison of bronchodilatory effect of theophhylline and the extract

There were no significant differences between the antiasthmatic effects (increased in PFTs) of two doses of boiled extracts (Fig. 3). There were also no significant differences between the effect of theophylline and those of both doses of extracts in first time intervals on most PFT values. The the increase in FEV_1, MMEF and MEF_{50} due to both doses of boiled extract and increase in MEF_{75} and MEF_{25} due to its lower doses in most later time intervals specially in last time intervals were significantly lower than those of theophylline ($p < 0.05$ to $p < 0.001$), (Fig. 3).

Discussion

In the present study the antiasthmatic effect of the boiled extract from *Nigella sativa* was compared to theophylline syrup.

Table 2
The baseline PFT (absolute values and percent predicted) of studied asthmatic patients in four different attendances and statistical differences between attendances.

PFTs	Theophylline		Extract (high dose)		Extract (low dose)		Salbutamol	
	Absolute	% pre	Absolute	% pre	Absolute	% pre	Absolute	% pre
FEV_1 (l)	2.32 ± 0.35	84.00 ± 7.95	2.14 ± 0.21	78.00 ± 6.31	2.23 ± 0.25	84.44 ± 7.5	2.10 ± 0.20	75.47 ± 5.65
MMF (l/s)	1.82 ± 0.36	51.40 ± 10.4	1.65 ± 0.23	47.46 ± 6.8	1.77 ± 0.31	51.5 ± 9.05	3.17 ± 0.34	46.24 ± 4.12
PEF (l)	3.46 ± 0.55	53.00 ± 5.70	3.18 ± 0.39	47.2 ± 3.52	3.68 ± 0.71	58.33 ± 7.61	1.71 ± 0.21	49.95 ± 6.06
MEF_{75} (l/s)	0.83 ± 0.15	48.5 ± 10.66	0.66 ± 0.09	38.38 ± 7.85	0.66 ± 0.14	44.66 ± 8.63	0.72 ± 0.12	44.41 ± 6.86
MEF_{50} (l/s)	2.19 ± 0.46	50.8 ± 10.89	2.03 ± 0.3	51.20 ± 6.88	2.45 ± 0.43	53.05 ± 12.37	1.99 ± 0.41	49.96 ± 6.23
MEF_{25} (l/s)	2.80 ± 0.45	45.00 ± 7.17	2.88 ± 0.42	46.33 ± 6.36	3.67 ± 0.57	61.22 ± 8.39	2.96 ± 0.48	48.82 ± 5.82
sGaw	0.17 ± 0.03		0.14 ± 0.04		0.13 ± 0.02		0.16 ± 0.06	

Data were presented in mean ± SEM (n=15). FEV1: forced expiratory volume in one second; PEF: peak expiratory flow; MMEF: maximal mid expiratory flow; SGaw: specific airways conductance; MEF_{75}, MEF_{50}, and MEF_{25}: maximal expiratory flow at 75, 50 and 25% of the FVC respectively; % pre: % predicted value.
There was not any significant difference in PFT Values between four attendances.

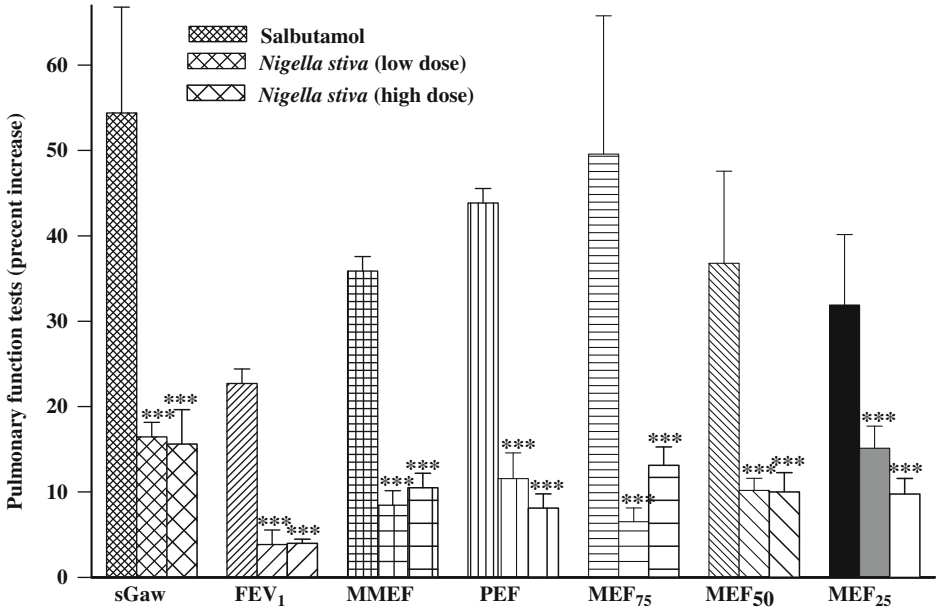

Fig. 2. The increase in pulmonary function tests (mean ± SEM) 30 min after administration of 200 μg inhaled salbutamol (fine filled bars), low (medium filled bars) and high doses (coarse filled bars) of *Nigella sativa* in studied asthmatic patients. Statistical differences between the effects of two doses of plant extract with those of inhaled salbutamol: ***; $p < 0.001$.

Table 3
Antiasthmatic effect of theophylline syrup (6 mg/kg) (% increase in different pulmonary function tests) on asthmatic airways (n=15) in different time intervals.

PFTs	30	60	90	120	150	180
FEV_1	8.58 ± 1.43**	17.38 ± 3.8***	24.48 ± 4.98***	28.54 ± 5.11***	27.95 ± 5.11***	22.69 ± 6.55***
MMEF	6.5 ± 1.03*	20.27 ± 4.26**	29.39 ± 6.07***	36.37 ± 7.8***	30.84 ± 6.37***	21.69 ± 6.39***
PEF	6.15 ± 1.51NS	19.76 ± 4.57***	25.29 ± 5.75***	22.33 ± 5.23***	19.47 ± 4.86***	15.81 ± 4.93***
MEF_{25}	10.34 ± 2.43***	31.7 ± 5.91***	38.91 ± 6.40***	41.45 ± 6.93***	43.96 ± 8.21***	41.27 ± 8.18***
MEF_{50}	21.54 ± 4.54***	36.68 ± 6.8***	42.94 ± 7.97***	41.52 ± 9.10***	35.94 ± 8.9 ***	30.29 ± 7.90***
MEF_{75}	12.92 ± 2.08***	24.56 ± 3.12***	28.45 ± 3.90***	28.52 ± 5.45***	24.57 ± 5.07***	16.27 ± 4.14***
sGaw	10.91 ± 3.75*	18.13 ± 5.42*	23.93 ± 7.83***	25.72 ± 8.58***	20.40 ± 6.54**	18.79 ± 4.75**

Statistical differences of increase in PFT values in different time intervals with baseline values using paired "t" test: NS; non significant difference, *; $p < 0.05$, **; $p < 0.01$, ***; $p < 0.001$. For other abbreviations see Table 1

Table 4
Antiasthmatic effect of higher dose of boiled extract (100 mg/kg) from *Nigella sativa* (% increase in different pulmonary function tests) on asthmatic airways (n=15) in different time intervals.

PFTs	30	60	90	120	150	180
FEV_1	3.85 ± 0.54***	4.87 ± 0.59***	5.94 ± 0.96***	5.46 ± 0.90***	4.47 ± 0.72***	4.30 ± 0.7***
MMEF	8.45 ± 0.96***	12.17 ± 1.86***	19.68 ± 1.89***	12.51 ± 2.08***	7.62 ± 1.08***	5.83 ± 1.05***
PEF	11.57 ± 3.00*	17.23 ± 3.10***	23.56 ± 4.23***	25.72 ± 5.11***	20.06 ± 5.54***	13.20 ± 5.38*
MEF_{25}	15.13 ± 2.57**	22.67 ± 4.27***	28.77 ± 6.08***	33.89 ± 6.42***	27.34 ± 6.51***	24.76 ± 6.38***
MEF_{50}	10.19 ± 1.41***	11.88 ± 1.66***	17.75 ± 1.79***	14.39 ± 1.42***	9.75 ± 1.62***	8.83 ± 1.79***
MEF_{75}	6.51 ± 1.62NS	10.00 ± 2.50**	16.53 ± 3.36***	18.87 ± 4.63***	5.60 ± 2.38NS	3.27 ± 1.54NS
sGaw	16.45 ± 2.3**	26.98 ± 5.13***	29.10 ± 5.30***	25.31 ± 5.20***	18.12 ± 4.34**	9.17 ± 2.78NS

For abbreviation see Table 2 and 3.

Table 5
Antiasthmatic effect of lower dose of boiled extract (50 mg/kg) from *Nigella sativa* (% increase in different pulmonary function tests) on asthmatic airways (n=15) in different time intervals.

PFTs	30	60	90	120	150	180
FEV_1	3.99 ± 0.48***	4.89 ± 0.55***	6.26 ± 0.76***	5.77 ± 0.74***	4.84 ± 0.70***	2.99 ± 0.66***
MMEF	10.49 ± 1.7***	12.02 ± 2.06***	16.10 ± 2.79***	14.42 ± 2.09***	8.20 ± 1.7**	4.02 ± 0.91NS
PEF	8.10 ± 1.67NS	10.65 ± 1.49**	15.91 ± 2.80**	19.58 ± 4.57***	17.54 ± 5.42**	13.93 ± 6.00*
MEF_{25}	9.76 ± 1.82***	11.52 ± 1.80***	14.09 ± 2.64***	11.22 ± 1.89***	9.68 ± 1.90***	8.61 ± 1.94***
MEF_{50}	10.01 ± 2.25**	10.55 ± 2.34**	15.34 ± 4.69***	12.86 ± 4.77***	9.75 ± 2.83*	4.31 ± 1.28NS
MEF_{75}	13.12 ± 2.15**	15.93 ± 2.97***	21.38 ± 3.86***	17.98 ± 4.79***	11.39 ± 3.45*	4.14 ± 1.8NS
sGaw	15.62 ± 4.03NS	23.9 ± 5.95**	34.14 ± 7.25***	31.83 ± 7.37***	25.30 ± 7.47***	27.93 ± 12.25**

For abbreviation see Table 2 and 3.

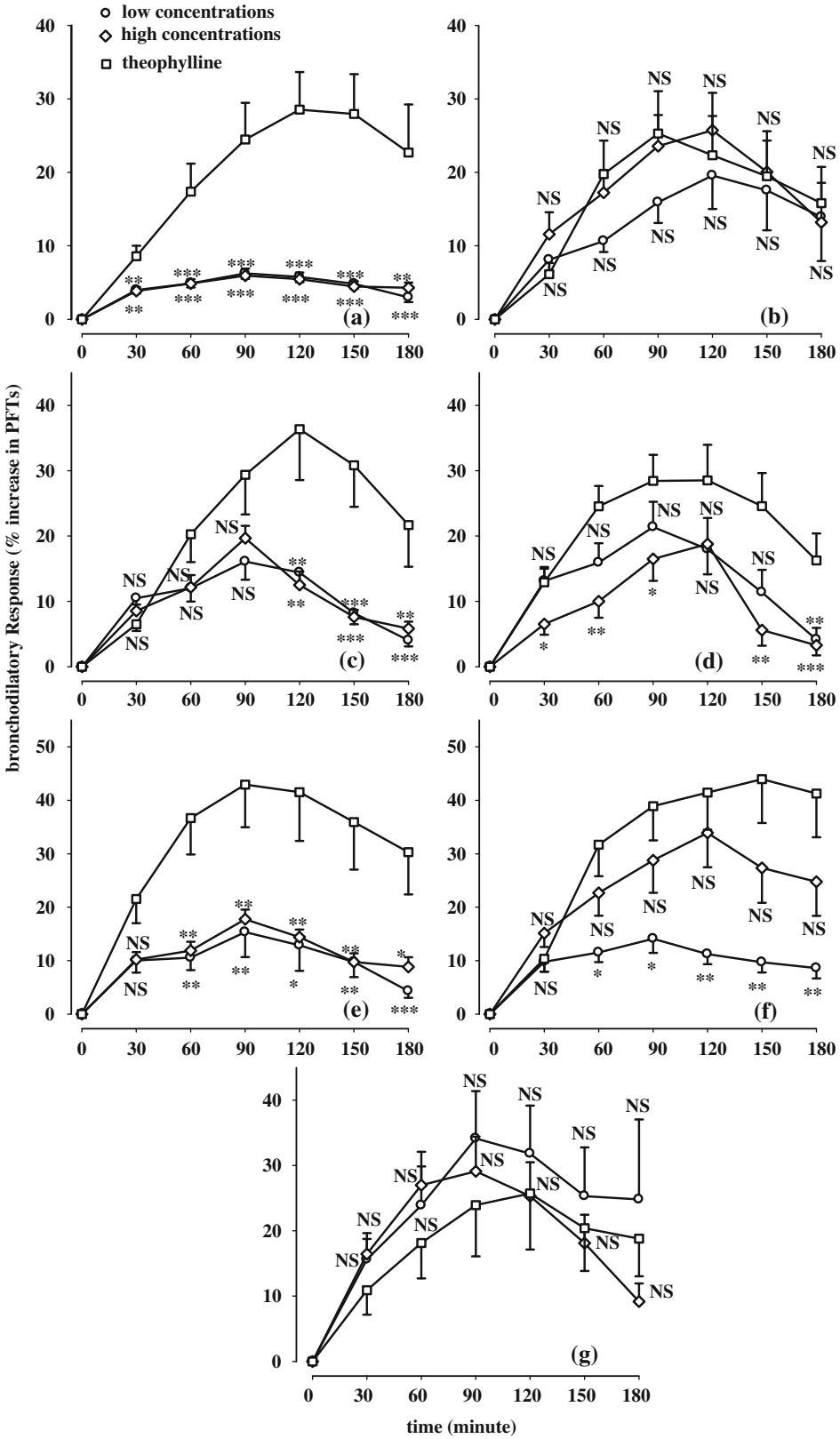

Fig. 3. Time response curves of the effect of theophylline syrup (□), 50 mg/kg (○) and 100 mg/kg (◇) of boiled extract from *Nigella sativa* on FEV_1 (a), PEF (b), MMEF (c), MEF_{75} (d), MEF_{50} (e), MEF_{25} (f), and sGaw (g), (% increase in different pulmonary function tests) in asthmatic airways. Statistical differences between the effects of two doses of plant extract with those of theophylline: NS: non significant difference, *; $p < 0.05$, **; $p < 0.01$, ***; $p < 0.001$. There was no any significant difference between the effect of two doses of extract from *Nigella sativa*.

The antiasthmatic effect of both drugs was examined by their effect on PFTs indicating airway diameter including: FEV_1, PEF, MMEF, MEF_{75}, MEF_{50}, MEF_{25} and sGaw. All PFTs measurements were performed by a final year Medical student, and patients were fully instructed about the required maneuvers before testing. The effect of salbutamol on PFTs was significantly greater

than those of both concentrations of the extract. However, in the present study, theophylline was used as an non specific bronchodilator control. In addition both the extract and theophylline were administered orally and the mode of phamacokiniytics is more similar than an inhaled drug.

The results showed a relatively potent antiasthmatic effect of boiled extract from *Nigella sativa.* In fact the extract caused significant increase in all measured PFTs. The antiasthmatic effect of the boiled extract was very similar to that of theophylline syrup in some regard at doses used. The onset of the antiasthmatic effect of the boiled extract was similar to that of theophylline syrup The antiasthmatic effect of the boiled extract from *Nigella sativa* and theophylline syrup began 30 min after administration. The effect of the boiled extract from *Nigella sativa* and theophylline declined 150 min after administration, but the rate of decline was greater for boiled extract. However, the effects of boiled extract from *Nigella sativa* on some PFTs (FEV_1, MMEF and MEF_{50}) were lower than those of theophylline. Therefore, the results of the present study showed a relatively potent bronchodilatory effect of the boiled extract from *Nigella sativa*. The smaller bronchodilatory effect of the boiled extract from *Nigella sativa* on some PFTs especially on FEV_1, MMEF and MEF_{50} may indicate that this plant has little effect on medium airways. In addition the duration of the antiasthmatic effect of boiled extract from *Nigella sativa* was slightly smaller than the effect of theophylline. The results of this study confirm those of previous studies indicating a relaxant effect of this plant on airway smooth muscle (Boskabady and Shahabi, 1997).

The non significant differences between the antiasthmatic effects of two concentrations may indicate that the maximum effect of boiled extract can occur at lower concentration. The reason for using boiled extract in the present study is that in Iranian traditional medicine this plant is used as this form of extract.

The mechanism(s) of antiasthmatic effect of *Nigella sativa* cannot be indicated by the results of the present study. Our previous studies indicated the anticholinergic (Boskabady and Shahabi, 1997), histamine (H_1) inhibitory effect (Boskabady and Shiravi, 2002), β-adrenegic stimulatory effect (Boskabady et al., 2004b), calcium channel inhibitory effect (Boskabady and Shirmohammadi, 2002) and potassium channel opening effect (Boskabady et al., 2004c) for this plant. Therefore, all or some of these mechanisms could contribute in its bronchodilatory. However, the greater effect of boiled extract from *Nigella sativa* on small airways may suggest the predominant β-adrenegic stimulatory effect for the plant because the density of β-adrenegic receptors is higher in small airways (Pendry, 1993). With regard to bronchodilatory effect of stimulation of inhibitory non adrenergic non cholinergic nervous system (NANC), inhibition of stimulatory NANC (Linden et al., 1993), and inhibition of phosphodiestrase (Van Amsterdam et al., 1989), all these mechanisms could contribute in the antiasthmatic effect of *Nigella sativa.* The contributions of these mechanisms on antiasthmatic effect of *Nigella sativa* should be clarified in further studies.

With regard to the existence of airway inflammation in the tracheobronchial tree of asthmatic patients, the antihistaminic effect of *Nigella sativa* might also prevent the inflammatory effect of histamine released from mast cells and basofill and have an anti-inflammatory effect, which would contribute to the therapeutic effect of this plant on asthma. In fact, the inhibitory effects of the essential oil of *Nigella sativa* and thymoquinone have been shown on both cyclooxygenase and 5-lipooxygenase pathways of arachidonic acid metabolism and also on membrane lipid peroxidation (Houghton et al., 1995). In addition the antitussive effect of *Nigella sativa* have been shown in our previous study (Boskabady et al., 2004a). Our recent study showed possible prophylactic effect of *Nigella sativa* seed extract in asthmatic patients (Boskabady et al., 2007). In fact tere are several evidences regarding anti-inflammatory activity of *N. sativa* (Hajhashemi et al., 2004), its therapeutic effect on patients with allergic diseases (allergic rhinitis, bronchial asthma, atopic eczema), (Kalus et al., 2003) and immunomodulatory effects of this plant (Labib Salem, 2005).

The effect of oral extract on pulmonary function tests was significantly less than inhaled salbutamol. Howver, the pharmacokinetics of an inhaled drug is completely different with that of oral drug. Inhaled drug acssess to aiorway smooth muscle almost directly and it is expected that the effect of inhaled drug on airway caliber should be greater than oral drug. In addition oral salbutamol usually cause tremore and increse heart rate and its oral administration is not easy in patients. Furthermore the effective ingredient of the plant may have greater effect on airway caliber of asthmatic patients. Therfore in further studies, it should be attempted to find out the effective substance of the plant and prepare its inhaled form and test it on PFT values of asthmatic pateints.

Therefore, as indicated in ancient Iranian medical books this plant could have therapeutic effects on respiratory diseases. However, more studies are required revealing the different therapeutic effect, effective substance(s), and mechanism(s) of action of *Nigella sativa.*

Although studied patients were on different types of medications, different types of medications of the patients do not affect the results because all tested drugs (theophylline and the extract) were tested in the same group in random order in 8 days.

With regard to variable airway diameter of asthmatic patients, the results of the present study showed consistent PFT values in studied patients in study time period. Therefore, the variable airway diameter do not affect the bronchodilatory effect of two doses of the extract and theophylline.

In conclusion, the results of the present study showed that *Nigella sativa* has a relatively potent antiasthmatic effect on asthmatic airways. However, the effects of boiled extract of this plant on most measured PFTs was less than those of theophylline at concentrations used.

Acknowledgements

This study was financially supported by Research Department of Mashhad University of Medical sciences. The authors would also like to thank Dr Sadeghnia for characterization of the extract by HPLC.

References

American Thoracic Society, 1995. Standardization of spirometry: 1994 update. Official statement of American Thoracic Society. Am. J. Respir. Crit. Car. Med. 152, 1107–1136.

Aqel, M.B., 1993. Effects of *Nigella sativa* seeds on intestinal smooth muscle. Inter. J. Pharmacogn. 31, 55–60.

Aqel, M.B., 1992. The relaxing effect of volatile oil of *Nigella sativa* seed on vascular smooth muscle. Jordan Ser. B 1, 91–100.

Ave-Sina, 1990. Law in Medicine (Sharafkhandy, A. (Interpreter)) Ministry of Guidance Publication, Theran, p. 314.

Boskabady, M.H., Javan, H., Sajadi, M., Rakhshandah, H., 2007. The possible prophylactic effect of *Nigella sativa* seed extract in asthmatic patients. Fund. Clinic. Pharmacol. 21, 559–566.

Boskabady, M.H., Kiani, S., Jandaghi, P., Ziaei, T., Zarei, A., 2004a. Antitussive of *Nigella sativa.* Pak. J. Med, Sci. 20, 224–228.

Boskabady, M.H., Kiani, S., Jandaghi, P., 2004b. Stimulatory effect of *Nigella sativa* on ß$_2$-adronceptors of guinea oig tracheal chains. Med. J. Islam. Rep. Iran. 18, 153–158.

Boskabady, M.H., Shahabi, M., 1997. Bronchodilatory and anticholinergic effects of *Nigella sativa* on isolated guinea-pig tracheal chains. Iran. J Med Sci. 22, 127–133.

Boskabady, M.H., Shirmohammadi, B., Jandaghi, P., Kiani, S., 2004c. Possible mechanisms for relaxant effect of aqueous and macerate extracts from *Nigella sativa* on tracheal chains of guinea pig. B. M. C. Pharmacol. 4, 3.

Boskabady, M.H., Shirmohammadi, B., 2002. Effect of *Nigella sativa* on isolated guinea pig tracheal chains. Arch. Iran. Med. 5, 103–107.

Boskabady, M.H., Shiravi, N., 2002. Inhibitory effect of *Nigella sativa* on histamine (H_1) receptors of isolated guinea pig tracheal chains. Pharmac. Biol. 40, 596–602.

El-Tahir, K.E.H., Ashour, M.M.S., Al-Harbi, M.M., 1993. The respiratory effect of the volatile oil of the Black seed (*Nigella sativa*) in guinea pig: elucidation of the mechanism(s) of action. Gen. Pharmacol. 24, 1115–1122.

Heaton, R.W., Gillett, M.K., Snashall, P.D., 1988. Morning–evening changes in airway responsiveness to methacholine in normal and asthmatic subjects; analysis using partial flow volume curves. Thorax 43, 727–728.

Hajhashemi, V., Ghannadi, A., Jafarabadi, H., 2004. Black cumin seed essential oil, as a potent analgesic and anti-inflammatory drug. Phytother. Res. 18, 195–199.

Houghton, P.J., Zarka, R., B, De las Heras, Hoult, J.R., 1995. Fixed oil of *Nigella sativa* and derived thymoquinone inhibit eicosanoid generation in leukocytes and membrane lipidperoxidation. Planta Med. 61, 33–36.

Kalus, U., Pruss, A., Bystron, J., Jurecka, M., Smekalova, A., Lichius, J.J., et al., 2003. Effect of *Nigella sativa* (black seed) on subjective feeling in patients with allergic diseases. Phytother. Res. 17, 1209–1214.

Labib Salem, M., 2005. Immunomodulatory and therapeutic properties of the *Nigella sativa* L. seed. Int. Immunopharmacol. 5, 1749–1770.

Linden, A., Lofdahl, C.G., Ullman, A., Skoogh, B.E., 1993. Non-adrenergic non-cholinergic responses stabilize smooth muscle tone with and without parasympathetic activation in guinea pig isolated airways. Eur. Respir. J. 6, 425–433.

Mahfouz, M., El-Dakhakhny, M., 1960. Chemical and pharmacological properties of the new anti-asthmatic drug, nigellone. Egypt Pharm. Bull. 42, 411–424.

Pendry, Y.D., 1993. Nural control of airways smooth muscle. Pharmacol. Ther. 57, 171–202.

Reiter, M., Brandt, W., Arzneim Forsch Drug Res, 1985. Relaxant effects on tracheal and ileal smooth muscles of the guinea-pig. Pharmacotherapy 35, 408–414.

Shefer,A.L., National Institutes of Health, 2002. Global strategy for asthma management and prevention: NHBLI workshop report. Bethesda, MD, January, Publication no. 02-3659.

Van Amsterdam, R.G.M., Meurs, H., Brouwer, F., Postema, J.B., Timmermans, A., Zaagsma, J., 1989. Role of phosphoinosited metabolism in functional antagonism of airway smooth muscle contraction by beta-adrenoceptor agonist. Eur. J. Pharmacol. 172, 175–183.