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Screening of several Indonesian medicinal plants for their inhibitory effect on histamine release from RBL-2H3 cells

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Abstract

Twelve alcoholic extracts and 12 hexane extracts of plant materials selected on the basis of medicinal folklore for asthma treatment in Indonesia were studied for their activity in inhibiting histamine release from RBL-2H3 cells (rat basophilic leukemia cell line), a tumor analog of mast cells. The results of screening indicated that five alcoholic extracts (*Plantago major* leaves, *Eucalyptus globulus* leaves and fruit, *Cinnamomum massoiae* cortex, *Vitex trifolia* leaves) and two hexane extracts (*Eucalyptus globulus* leaves, *Vitex trifolia* leaves) inhibited IgE-dependent histamine release from RBL-2H3 cells. The inhibitory effects were found to be more than 80% for extract concentrations of 0.5 mg/ml. The results indicate that the extracts contain active compounds that inhibit mast-cell degranulation, and provide insight into the development of new drugs for treating asthma and/or allergic disease. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Histamine; Indonesian medicinal plants; Jamu; RBL-2H3 cells

1. Introduction

The mechanism of the inflammatory response resulting in asthma is complex and involves numerous cell types, including mast cells (Meltzer, 1998). The mast cell has long been associated with asthma, since it releases a variety of preformed and newly synthesized mediators that could account for several features of asthma (Barnes, 1993). Among the mediators released from mast cells, histamine is a well-characterized and the most potent vasoactive mediator in acute bronchoconstriction provoked by allergen, exercise, hypertonic stimuli and inhaled adenosin. Histamine may also contribute to the allergen-induced late asthmatic response probably following the recruitment and activation of basophils (Holgate, 1999).

Rat basophilic leukemia (RBL-2H3) cells, a tumor analog of mast cells, display properties of mucosal-type mast cells. The 2H3 cells contain several hundred thousand IgE receptors on the membrane surface, and after sensitization with mouse monoclonal IgE, the cells respond to antigen and release histamine. Although the mucosal mast-cell response to secretagogues and their sensitivity to inhibitors are different from those of cutaneous-type mast cells, the mechanism of histamine secretion is supposed to be general (Maeyama et al., 1992). Their advantage over peritoneal mast cells is that a great number of homogenous cells are obtained at once and can be used for experiments. They thus provide a good tool for studying the effect of unknown compounds on histamine release activity.

The use of herbal medicines has increased in recent years. Many medicinal plants provide relief of symptoms comparable to that obtained from allopathic medicines. Specific chemical derivatives have been isolated from many plant products that act on the mechanisms and mediators that cause asthma and allergies (Bielory and Lupoli, 1999). In Indonesia, several medicinal plants have been traditionally used in the treatment of respiratory disorders. These plants are: *Amomum cardamomum* Willd, *Cinnamomum burmanii* Nees ex BL, *Cinnamomum massoiae* Schewc, *Curcuma xanthorrhiza* Roxb, *Eucalyptus globulus* Labill, *Justicia gendarusa* Linn, *Orthosiphon stamineus* Benth, *Plantago*

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major L., *Piper cubeba* L.f., *Thymus vulgaris* L., and *Vitex trifolia* L. Some of these plants have been reported to have tracheospasmolytic activity on guinea-pig trachea contraction induced by histamine and other spasmogens, whereas for others, no scientific data concerning their activities for asthma therapy have been reported.

Broucke and Lemli (1983) and Meister et al. (1999)reported the spasmolytic activity of *Thymus vulgaris* on guinea-pig isolated trachea. Such an effect is also found in *Piper cubeba*, *Vitex trifolia*, *Curcuma xanthorrhiza*, and *Eucalyptus globulus* (Wahyuono et al., 1998, 1999). The spasmolytic or bronchodilator effect is only one action of an anti-asthma drug due to the complexity of the disease. Other actions involve protection of the airways from precipitants that lead to bronchospasm or inflammation and contribute towards resolving airway inflammation (Szefler, 1993). Inhibition of mast-cell degranulation, which in turn inhibits release of mast-cell mediators, is also considered one means of treating asthma, as shown by the cromones drugs, such as sodium cromoglycate and nedocromil sodium, the most specific anti-allergic drugs discovered so far (Barnes, 1999).

Investigation of how traditionally used medicinal plants work is one way of discovering bioactive compounds (Verpoorte, 1999). In this study, we screened medicinal plants regarding their effects on histamine release from mast-cell models, believed to be one of the triggering events of allergic asthma disease. We discussed whether the plants have a significant effect on asthma therapy and whether there is synergism between the bronchospasmolytic activity and the inhibitory effect of histamine release of the medicinal plants. The results of this screening may provide useful information for further discovering pharmacologically active compounds for treatment of asthma.

2. Materials and methods

2.1. Plant collection

Eleven types of plants that are commonly used in "jamu" (traditional Indonesian medicine) as remedies for asthma or respiratory disorders were selected. These plant materials were collected from the plantation in the Medicinal Plants Research Office (BPTO), Tawangmangu, Surakarta, Indonesia. These plant materials were identified by a botanist at the BPTO, Tawangmangu, and their voucher specimens were deposited in the Department of Pharmacognosy, Faculty of Pharmacy, Gadjah Mada University, Yogyakarta, Indonesia. The names of these medicinal plants, voucher numbers, and parts of each plant used for the experiments are listed in Table 1.

2.2. Preparation of medicinal plant extracts

The plant material was cut into small pieces and dried in an oven set at 50°C. The dried material was ground into powder, which was then extracted with n-hexane followed by ethanol to give n-hexane and ethanol extracts, respectively.

In brief, the powder obtained from each plant (500 g each) was macerated with 250 ml of n-hexane overnight. After filtration and evaporation of the filtrate, dried n-hexane extracts were obtained. This maceration procedure was performed twice. Maceration of the residual plant was then continued with ethanol,

Table 1
Medicinal plants used for asthma remedies in traditional Indonesian medicine (Jamu)

No.	Names of medicinal plant	Voucher number	Code	Part of the plant used	Weight (g)		
					Dried powder (g)	n-hexane extracts	Ethanol extracts
1.	*Amomum cardamomum* Willd	BF 804	AC	Fruit	500	24.65	7.35
2.	*Cinnamomum burmanii* Nees ex BL	BF 806	CB	Cortex	500	4.03	85.83
3.	*Cinnamomum massoiae* Schewc	BF 807	CM	Cortex	500	25.55	25.15
4.	*Curcuma xanthorrhiza* Roxb	BF 811	CX	Rhizomes	500	20.77	16.40
5.	*Eucalyptus globulus* Labill	BF 811	EGL	Leaves	500	22.58	42.49
6.	*Eucalyptus globulus* Labill	BF 814	EGF	Fruit	500	24.15	95.55
7.	*Justicia gendarusa* Linn	BF 816	JG	Leaves	500	14.26	23.92
8.	*Orthosiphon stamineus* Benth	BF 817	OS	Leaves	500	4.92	25.92
9.	*Piper cubeba* L.f.	BF 819	PC	Fruit	500	82.97	30.57
10.	*Plantago major* L.	BF 820	PM	Leaves	500	6.72	30.70
11.	*Thymus vulgaris* L.	BF 823	TV	Leaves	500	19.80	51.49
12.	*Vitex trifolia L.*	BF 801	VT	Leaves	500	22.49	40.12

and ethanol extracts were obtained by the procedure as described above.

2.3. Materials

Dinitrophenylated bovine serum albumin (DNP_{24}-BSA, which consists of 24 mol of dinitrophenol bound per 1 mol of BSA) was a gift from Dr. H. Metzger, NIH (Bethesda, MD). Monoclonal IgE against DNP-BSA was purified from the supernatant in IgE producing hybridoma, which was obtained in our laboratory. Eagle's minimum essential medium (MEM) and antibiotics were obtained from Gibco (Grand Island, NY), fetal calf serum was purchased from JRH Biosciences (A SCL company), and PIPES [piperazine-1,4-bis(2-ethanesulfonic acid)] was purchased from Dosindo (Kumamoto, Japan). Other chemicals were of the highest grade available.

2.4. Preparation of RBL-2H3 cells line

RBL-2H3 cells were cultured in MEM containing 15% fetal calf serum in a flask in a humidified atmosphere of 5% of CO_2 in air at 37°C according to Barsumian et al. (1981). For the histamine release assay, RBL-2H3 cells were seeded into 24-well culture plates (2×10^5 cells/well) in 0.4 ml medium for each well. Cells were incubated overnight at 37°C and sensitized with 0.5 μg/ml of monoclonal IgE against DNP_{24}-BSA.

2.5. Assay of histamine release

After sensitizing the cells with IgE, the medium was removed, and the cells were washed twice with 0.5 ml of PIPES buffer (25 mM PIPES, 119 mM NaCl, 5 mM KCl, 5.6 mM glucose, 0.4 mM $MgCl_2$, 1 mM $CaCl_2$, 40 mM NaOH, 0.1% BSA, pH 7.2) and preincubated with either 200 μl of PIPES buffer (as control) or extracts of medicinal plants (concentration 0.5 mg/ml) at 37°C for 10 min. For comparison, quercetin (50 μM) and thapsigargin (0.5 μM) were used as a standard for inhibitory effect and stimulatory effect, respectively. RBL-2H3 cells were stimulated with 20 ng/ml of DNP_{24}-BSA as antigen for 30 min, and histamine released into the medium was measured by HPLC-fluorometry according to Yamatodani et al. (1985).

Briefly, 100 μl of the cell medium were collected and centrifuged at 3000 rpm for 5 min. Fifty microlitres of supernatant were then collected and diluted with 250 μl of 3% perchloric acid in 5 mM Na_2EDTA and added by 30 μl 2 M KOH/1 M KH_2PO_4. This mixture was then centrifuged at 10 000 × *g* for 15 min at 4°C, and 50 μl of the supernatant were injected directly onto a column packed with TSKgel SP-2SW Cation Exchanger (Tosoh, Tokyo). Histamine was eluted with 0.25 M potassium phosphate at a flow rate of 0.6 ml/min. The histamine was post-labeled with *o*-phthalaldehyde in alkaline conditions, and detected fluorometrically in an F1080 Fluorometer (Hitachi, Tokyo), using excitation and emission wavelengths of 360 and 450 nm, respectively.

The percentage of net histamine release was calculated as follows:

$$\text{Net histamine release (\%)} = \frac{\text{challenged release (pmol)} - \text{spontaneous release (pmol)}}{\text{total histamine (pmol)} - \text{spontaneous release (pmol)}} \times 100.$$

Spontaneous histamine release is the release of histamine in the absence of DNP-BSA antigen, and it was calculated with the following equation:

$$\text{Spontaneous histamine release (\%)} = \frac{\text{histamine release (pmol)}}{\text{total histamine content (pmol)}} \times 100.$$

The inhibition percentage of histamine release was calculated using the following equation:

$$\text{Percentage inhibition} = \frac{\text{histamine release without drugs} - \text{histamine release with drugs}}{\text{histamine release without drugs}} \times 100.$$

3. Results

3.1. Extraction of medicinal plants

Each of the medicinal plant materials was extracted using the procedure described in Fig. 1, and the yields of each extract are reported in Table 1.

3.2. Effect of the extracts on histamine release

A total of 24 extracts derived from 11 different plant species commonly used in traditional Indonesian medicine to treat respiratory disorders were screened for their inhibitory effect on histamine release in RBL-2H3 cells. Histamine release from IgE-sensitized RBL-2H3 cells was induced by DNP-BSA as antigen stimulation. The net histamine release from RBL-2H3 effected by medicinal plant extracts is shown in Fig. 2a and b, for hexane and ethanol extracts, respectively. The inhibition of histamine release by the extracts is shown in Table 2.

Extracts were considered as having a high, medium or low activity if inhibition of histamine release was more than 80%, between 40 and 80% or less than 40% compared to the control treatment, respectively. Two

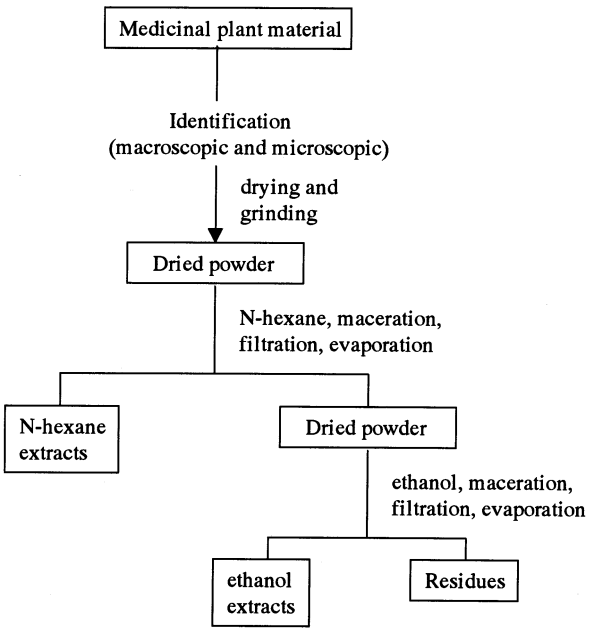

Fig. 1. Scheme of procedures for obtaining n-hexane and ethanol extracts from the medicinal plants.

n-hexane extracts and five ethanol extracts were found to have high inhibitory effects on histamine release from 2H3 cells showing more than 80% inhibition of histamine release compared to controls, whereas quercetin (50 μM) as a standard drug showed an inhibition of about 80% (Table 2). The extracts with a high inhibitory activity (in alphabetical order) are as follows: n-hexane extracts of *Eucalyptus globulus* (leaves) and *Vitex trifolia* (leaves), and ethanol extracts of *Cinnamomum massoiae* (cortex), *Eucalyptus globulus* (leaves and fruit), *Plantago major* (leaves), and *Vitex trifolia* (leaves). Other plant extracts showed either a medium or low inhibitory activity.

We also found evidence for varying levels of induction of histamine release by some medicinal plant extracts, even though no antigen was added. The effect was considered significant if the extracts caused spontaneous histamine release of more than 10%. Thapsigargin, as a standard drug, showed stimulation of histamine release of about 65%. Extracts having such an effect are: both n-hexane and ethanol extracts of *Cinnamomum burmanii* cortex, *Curcuma xanthorriza* rhizome, and *Piper cubeba* fruits; hexane extracts only of *Eucalyptus globulus* fruits and *Cinnamomum massoiae* cortex; and ethanol extracts of *Orthosiphon stamineus* leaves. The percentage of spontaneous histamine release induced by the extracts is shown in Table 3.

4. Discussion

Asthma is defined as a lung disease with the following characteristics: (1) airway obstruction that is reversible, but not completely so in some patients; (2) airway inflammation; and (3) increased airway responsiveness to a variety of stimuli (Busse and Reed, 1993). Therapeutic strategies for asthma include bronchodilators, corticosteroids, mediator antagonists (antihistamines, antileukotrienes, etc.), anti-inflammatory drugs, and specific inhibitors drugs, such as cromones that act by inhibiting mast-cell degranulation, etc. (Barnes, 1999).

Recently, the use of herbal medicine as an alternative medicine for the treatment of various diseases (Bielory and Lupoli, 1999), including asthma, has increased dramatically. The use of herbal medicines is based on traditional healing, and is also influenced by culture. In Indonesia, the use of medicinal plants and herbal therapy has been practised long before recorded history. However, scientific knowledge concerning the mechanism of action of medicinal plants in asthmatic disease is very limited. It is likely that some of the plants used have no significant effect on respiratory disorders.

In this study, we investigated several medicinal plant extracts traditionally used in Indonesia for asthma therapy, and focused our attention on their inhibitory action against histamine release from mast cells. We used quercetin as a standard drug for an inhibitory effect, since the 2H3 cells are insensitive to commonly used mast-cell stabilizers like sodium cromoglycate or nedocromil (Maeyama et al., 1992). Quercetin, a naturally occurring flavonoid found in many plants, has been reported to potently inhibit histamine release from rat peritoneal mast cells (Fewtrell and Gomperts, 1977) and 2H3 cells (Cheong et al., 1998) by inhibiting protein kinase (Hagiwara et al., 1988). For the stimulatory effect, we used thapsigargin, a sesquiterpen lacton isolated from the roots of *Thapsia garganica*, L., which is known to release histamine from mast cells (Patkar et al., 1979) by inhibiting the sarcoplasmic/endoplasmic reticulum (ER) calcium-dependent ATPase (Thastrup et al., 1994) that in turn elevates cytosolic Ca^{2+} required to induce histamine release from mast cells. The results of screening were also then compared to the known effects of the medicinal plants on bronchospasmolytic activity (Table 4) for further discussion.

Histamine and mast cells are of our interest, since they are closely related to asthmatic disease, and drugs acting on mast cells may be effective as a prophylactic agent in the treatment of mild to moderate asthma, although the precise mechanism of action is not completely understood (Meltzer, 1998). It is best to begin treatment prophylactically and prevent the onset of significant symptomatology rather than attempting to lessen the ongoing symptoms (Meltzer, 1998).

Some of the medicinal plants were found to suppress histamine release from 2H3 cells to various extents (Table 2). Interestingly, we found that some extracts also had an opposite effect, i.e. they both inhibited histamine release and induced spontaneous histamine release, as found in hexane and ethanol extracts of *Cinnamomum bumanii* and ethanol extracts of *Orthosiphon stamineus*. In such cases, it is difficult to derive any exact conclusions concerning the inhibitory effect of these plants, since the opposite effects were mixed. This phenomenon is likely to happen since there are still various compounds and these require more separation.

We also noted that some plants did not have any considerable inhibitory effect and even induced spontaneous histamine release, as in the case of hexane and ethanol extracts of *Curcuma xanthorrhiza* and *Piper cubeba*. The mechanism of induction of histamine release from 2H3 cells by these extracts has not yet been investigated. One possibility is that the plant caused cell

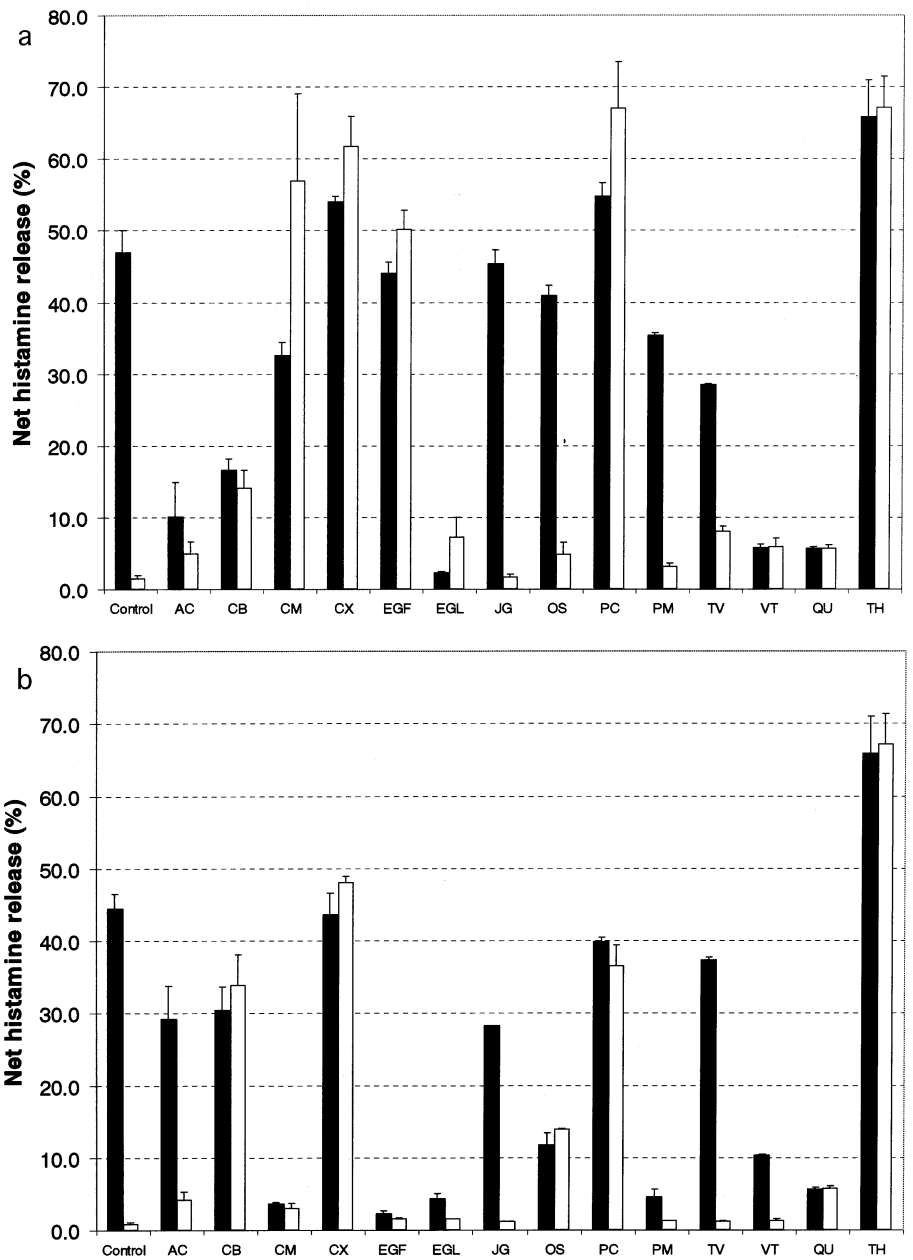

Fig. 2. Effect of n-hexane extracts (a) and ethanol extracts (b) of medicinal plants on histamine release activity from 2H3 cells either in the presence (solid bar) or absence (open bar) of DNP-BSA as antigen to stimulate histamine release. Each of the data represents mean ± S.E.M of three experiments performed in duplicate ($n = 6$). Note that several medicinal plants induced significant spontaneous histamine release in the absence of antigen. The names of the medicinal plant were coded as shown in Table 1. QU is quercetin 50 μM, and TH is thapsigargin 0.5 μM for the standard drug.

Table 2
Inhibition of histamine release from 2H3 cells by the medicinal plants[a]

Names of medicinal plants	Parts of the plant	Inhibition of histamine release[b] (%)	Extract solvent	Spontaneous histamine release
Quercetin (50 μM)		81.24 ± 4.25		
With >80% effect				
Eucalyptus globulus Labill	Leaves	84.85 ± 6.18	Hexane	None
Vitex trifolia L.	Leaves	80.13 ± 3.95	Hexane	None
Cinnamomum massoiae Schewc	Cortex	90.78 ± 0.34	Ethanol	None
Eucalyptus globulus Labill	Fruit	93.21 ± 1.42	Ethanol	None
Eucalyptus globulus Labill	Leaves	85.39 ± 1.70	Ethanol	None
Plantago major L.	Leaves	87.61 ± 0.57	Ethanol	None
Vitex trifolia L.	Leaves	81.58 ± 0.24	Ethanol	None
With 40%>effect>80%				
Amomum cardamomum Willd	Fruit	66.85 ± 6.49	Hexane	None
Cinnamomum burmanii Nees ex BL	Cortex	62.97 ± 0.82	Hexane	Induced
Thymus vulgaris L.	Leaves	46.22 ± 0.08	Hexane	None
Justicia gendarusa Linn	Leaves	41.78 ± 0.01	Ethanol	None
Orthosiphon stamineus Benth	Leaves	73.20 ± 2.59	Ethanol	Induced
With <40% effect				
Cinnamomum massoiae Schewc	Cortex	38.79 ± 3.44	Hexane	Induced
Curcuma xanthorrhiza Roxb	Rhizomes	−0.91 ± 1.41	Hexane	Induced
Eucalyptus globulus Labill	Fruit	17.01 ± 3.36	Hexane	Induced
Justicia gendarusa Linn	Leaves	15.19 ± 3.64	Hexane	None
Orthosiphon stamineus Benth	Leaves	23.28 ± 2.53	Hexane	None
Piper cubeba L.f.	Fruit	−3.45 ± 3.08	Hexane	Induced
Plantago major L.	Leaves	33.54 ± 0.61	Hexane	None
Amomum cardamomum Willd	Fruit	36.50 ± 7.30	Ethanol	None
Cinnamomum burmanii Nees ex BL	Cortex	35.54 ± 5.49	Ethanol	Induced
Curcuma xanthorrhiza Roxb	Rhizomes	8.35 ± 4.77	Ethanol	Induced
Piper cubeba L.f.	Fruit	15.85 ± 1.22	Ethanol	Induced
Thymus vulgaris L.	Leaves	23.30 ± 0.92	Ethanol	None

[a] Data represent the mean ± S.E.M of three experiments performed in duplicate ($n = 6$), as a percentage of inhibition.
[b] Inhibition of histamine release by the medicinal plants was calculated using the equation mentioned in Section 2.5.

lysis, as found in hexane extracts of *Piper cubeba*. However, other mechanisms are possible and require further investigation.

In this study, we rather prefer to discuss the possible correlation between the inhibitory effect on histamine release and bronchospasmolytic activity of the medicinal plants. We found that inhibition of histamine release was not correlated with bronchospasmolytic activity, and some extracts even demonstrated the opposite effect. We classified our findings into three categories. Plants in the first category have both bronchospasmolytic activity and an inhibitory effect on histamine release. In this category are *Eucalyptus globulus* leaves (ethanol extract) and *Vitex trifolia* leaves (both n-hexane and ethanol extracts). This dual action may be due to the presence of various compounds in those plants that may have a significant effect on asthma therapy.

Plants in the second category have bronchospasmolytic activity, but only a mild or no effect on histamine release from 2H3 cells. This category includes *Thymus vulgaris* leaves. This plant has long been used for the treatment of coughs, and it has been reported to have bronchospasmolytic activity (Broucke and Lemli, 1983; Meister et al., 1999). Both n-hexane and ethanol extracts of this plant showed inhibition of histamine release of less than 40%.

Plants in the third category show bronchospasmolytic activity, but also induce spontaneous histamine release from 2H3 cells. This category includes *Piper cubeba* (fruit) and *Curcuma xanthorrhiza* (rhizome). Both n-hexane and ethanol extracts from these plants strongly induced histamine release from 2H3 cells, even though no antigen was added. This evidence for these opposite actions suggests that there are various active compounds in the plant extracts, and further isolatation and purification are still required to find the pure active compound that is most effective in the treatment of asthma. Several investigators have reported that the rhizome of *Curcuma xanthorrhiza* has anti-inflammatory activity (Ozaki, 1990; Claeson et al., 1996). It would be reasonable to expect that plants with an

Table 3
Spontaneous histamine release induced by several medicinal plants[a]

Names of medicinal plant	Part of the plant used	Extract solvent	
		n-hexane	Ethanol
Thapsigargin (0.5 μM)		66.40 ± 4.31	
Cinnamomum burmanii Nees ex BL	Cortex	14.05 ± 2.51	33.83 ± 4.23
Cinnamomum massoiae Schewc	Cortex	56.86 ± 12.17	None
Curcuma xanthorrhiza Roxb	Rhizomes	61.71 ± 4.25	47.99 ± 0.86
Eucalyptus globulus Labill	Fruit	50.17 ± 2.59	None
Orthosiphon stamineus Benth	Leaves	None	13.92 ± 0.18
Piper cubeba L.f.	Fruit	67.04 ± 6.41	36.47 ± 2.89

[a] Data represent the mean ± S.E.M of three experiments performed in duplicate ($n = 6$), as a percentage. The percentage of spontaneous histamine release was calculated using the equation mentioned in Section 2.5.

anti-inflammatory effect would inhibit histamine release from mast cells. However, we did not find any evidence that this plant inhibited histamine release from mast cells, and it is likely that the site of action on the target cells is different. In fact, we found that the extract from *Piper cubeba* caused lysis of 2H3 cells, and this may account for the high histamine release.

There is no other available literature concerning the bronchospasmolytic activity of the other medicinal plants, apart from that shown in Table 4. To our knowledge, our report is the first concerning the effects of Indonesian medicinal plants on the activity of histamine release from 2H3 cells.

The mechanism of histamine release from 2H3 cells involves several pathways. The cascades responsible for release have been considered to involve aggregation of IgE receptors (Maeyama et al., 1986), tyrosine phosphorylation of phospoliphase C (Park et al., 1991) via *src*-related tyrosine kinase (Jouvin et al., 1994), hydrolysis of inositol phospholipids (Maeyama et al., 1988), and mobilization of calcium by generated inositol triphospate (Streb et al., 1983), enhanced calcium influx from the cell exterior (Beaven et al., 1984) and production of diacylglycerol (Nishizuka, 1984). The final two messengers, calcium signal and activation of protein kinase C, then elicit the release of histamine synergistically (Beaven et al., 1987).

Table 4
Medicinal plants reported to have bronchospasmolytic activity

Names of medicinal plant	Part of the plant used	References
1. *Curcuma xanthorrhiza* Roxb	Rhizomes	Wahyuono et al., 1998
2. *Eucalyptus globulus* Labill	Leaves	Wahyuono et al., 1998
3. *Piper cubeba* L.f.	Fruit	Wahyuono et al., 1999
4. *Thymus vulgaris* L.	Leaves	Broucke and Lemli, 1983; Meister et al., 1999
5. *Vitex trifolia* L.	Leaves	Wahyuono et al., 1998

The inhibitory action of the medicinal plants against histamine release from 2H3 cells has not yet been investigated and might influence one or more of these proposed mechanisms. Further study is required to investigate the mechanism by which the medicinal plants inhibit histamine release from mast cells. Isolation and purification of some potent extracts are being carried out by our group for such purposes. If this mechanism is also applied in an in-vivo experiment, it would provide useful information to further explain drug action.

We conclude that some of the Indonesian medicinal plants traditionally used for asthma treatment might have significant effects on mast-cell degranulation and provide insight for the discovery of new drugs for treating respiratory disorders involving mast cells.

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