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Investigation of Anti-Asthmatic effects of *Syzyzium Cumini* Flesh of the Fruit on Guinea Pig Tracheal chains and its Possible Mechanism(s)

P. K. Mahapatra* & D. Pradhan
Pharmacology Division, University Department of Pharmaceutical Sciences, Utkal University, Bhubaneswar, Odisha, India.

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ABSTRACT

Syzygium cumini (Family Myrtaceae) is also known as Syzygium jambolanum and Eugenia cumini. Other com-mon names are Jambul, Black Plum, Java Plum, Indian Blackberry, Jamblang, Jamun etc. Today these trees are found growing throughout the Asian subcontinent, East-ern Africa, South America, Madagascar and have also naturalized to Florida and Hawaii in the United States of America [1]. The tree fruits once in a year and the berries are sweetish sour to taste. The ripe fruits are used for health drinks, making preserves, squashes, jellies and wine [1]. In association to itsdietary use, all parts of the tree and, importantly the seeds are used to treat a range of ailments, the most important being diabetes mellitus [2]. Different parts of the jambolan were also reported for its antioxidant, anti-inflammatory, neuropsycho-phar- macological, anti-microbial, anti-bacterial, anti-HIV, an-tileishmanial and antifugal, nitric oxide scavenging, free radical scavenging, anti-diarrheal, antifertility, anorex-igenic, gastroprotective and anti-ulcerogenic and redio-protective activities [2]. The purpose of this study was investigating experimentally the possible anti asthma activity of macerated and soxhlet extracts of fruits of this plant on tracheal chains of guinea pigs were evaluated. The relaxant effects of 4 cumulative concentrations of macerated and soxhlet extracts (0.25, 0.5, 0.75, 1.0and 1.25 W/V) in comparison with saline as negative control and 4 cumulative concentrations of theophylline (0.25, 0.5, 0.75, 1.0 and 1.25 mM) as positive control were examined on precontracted tracheal chains of two groups of 6 guinea pig by 60 mM KCl (group 1, N=6) and 10 µM methacholine the non-incubated tissues (group 2, N = 6) and tissues incubated with 1 µM propranolol (group 3, N = 4) [18]. Decrease in contractile tone of tracheal chains was considered as relaxant effect. The isolated guinea-pig trachea pre-contracted with KCl, methacholine and tissues incubated with propranolol were used to study the relaxation of macerated and soxhlet extracts of fruits Syzygium cumini. In group 1 experiments only the last two higher concentrations of theophylline and soxhlet extract showed significant relaxant effect compared to that of saline (p<0.001 for both concentrations), which were significantly greater than those of macerated extracts (p<0.001 for all cases). In group 2 experiments only the last two higher concentrations of theophylline and soxhlet extract showed significant relaxant effect compared to that of saline. The effects of one higher concentrations of theophylline in this group were significantly greater than those of macerated and soxhlet extracts (P < 0.01). And in group 2 and 3 experiments both macerated and soxhlet extracts showed concentration-dependent relaxant effects compared to that of saline (p<0.05 to p<0.001 for both extracts).The relaxant effects of macerated and soxhlet extracts in group 1 were significantly lower than those of groups 2 and 3.In group 3 experiment potent relaxant effect was observed.

Keywords: *Syzygium cumini, Bronchodilatory, Guinea pig. Trachea.*

INTRODUCTION

Myrtaceae is a plant family widely used in folk medicine in different countries and *Syzygium cumini* is a evergreen plant is originally from Indonesia and India, belongs to the Myrtaceae family. All parts of the plant can be used medicinally and it has a long tradition in alternative medicines. The leaf has anti-flammatory activity [1], the *fruit* has Hypoglycemic, anti-flammatory, anti arthritic and anti pyretic activity [4], respiratory diseases [6], and allergic disorders [6] and used in India for anemia, antibioticactivity. The ethanolic bark extract has been reported to have anti-inflammatory activity in carrageenan and formaldehyde paw edema [5]. The same extract was also shown to inhibit histamine-, serotonin (5-HT) and prostaglandin 2-induced paw edema [7]. The allergic process has an important inflammatory component in which mast cell activation and degranulation are the first phenomena observed. During this process, mast cells release several inflammatory me-diators including histamine, 5-HT, platelet-aggregating factor (PAF), leukotrienes, and a variety of cytokines which can elicit many events associated with allergic inflammation, such as edema formation and cellular infiltration [8]. Fruit juice for gingivitis and also used against diarrhea and fever. Fruits used for diabetes which reduce the blood sugar level quickly. It also used against diarrhea & abdominal pains, skin diseases [9] leucorrhoea & general debility. *Fruits* give orally reduced blood sugar & glycosuria in patients. Powdered *fruits* are used as a remedy in diabetes and in metrorrhagia. Extract of *fruits* of *S.cumini* were found to have antidiabetic, antiinflammatory, hepatoprotective, antihyperlipidemic, diuretic and antibacterial activity. These properties of *S.cumini leaves* have been attributed to its saponins, tannin and flavonoids. These medicines are free from side effects and cheap compared to allopathic medicines, but still common people/educated people do not use them as they are prepared & practiced by the traditional medical practitioners [9-12]. Flavonids prevent oxidative cell damage suggesting antiseptic, anticancer, anti-inflammatory effects and mild hypersensitive properties. The jambolan is fast-growing, reaching full size in 40 years. It ranges up to 100 ft (30 m) in India and Oceania, up to 40 or 50 ft (12-15 m) in Florida, and it may attain a spread of 36 ft (11 m) and a trunk diameter of 2 or 3 ft (0.6-0.9 m). It usually forks into multiple trunks a short distance from the ground. The bark on the lower part of the tree is rough, cracked, flaking and discolored, further up it is smooth and light-gray. The turpentine-scented evergreen leaves are opposite, 2 to 10 in (5-25 cm) long, 1 to 4 in (2.5-10 cm) wide, oblong-oval or elliptic, blunt or tapering to a point at the apex, pinkish when young, when mature, leathery, glossy, dark-green above, lighter beneath, with conspicuous, yellowish midrib. The fragrant flowers, in 1-to 4-in (2.5-10 cm) clusters, are 1/2 in (1.25 cm) wide, 1 in (2.5 cm) or more in length, have a funnel-shaped calyx and 4 to 5 united petals, white at first, then rose-pink, quickly shed leaving only the numerous stamens. *Syzygium cumini* tree about 8 to 15 meters high with white branches and reddish young shoots. Leaves are opposite, shiny and leathery, oblong-ovate to elliptic or obovate-elliptic, 6 to 12 centimeters long, the tip being broad and shortly pointed. Panicles are borne mostly from the branchlets below the leaves, often being axillary or terminal, about 4 to 6 centimeters long. Flowers are small, numerous, scented, pink or nearly white, in clusters, without stalks, borne in crowded fascicles on the ends of the branchlets. Calyx is funnel-shaped, about 4 millimeters long, and 4-toothed. Petals cohere and fall all together as a small disk. Stamens are numerous and about as long as the

***Corresponding author:**
Prasanta Kumar Mahapatra
Pharmacology Division,
University Department of Pharmaceutical Sciences,
Utkal University, Bhubaneswar, Odisha, India. Phone: 9000261204
**E-Mail: hihi8786@gmail.com*

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calyx. Leaves are oval to elliptic, 1.5 to 3.5 centimeters long, dark purple or nearly black, luscious, fleshy and edible with a sweet astringent taste; containing a single large leaves [13]. The seeds are astringent,diuretic, stops urinary discharge and remedy for diabetes and the barks showed good wound healing properties(Nadkarni, 1954). Syzygium cuminiis a medicinalplant, whose parts were pharmacologically provedto possess hypoglycemic, antibacterial, anti-HIV activityand anti-diarrhea effects. (Bhuiyan et al., 1996; Kusumoto et al.,1995; Indira and Mohan, 1993). Slowing et al. (1994) and Muruganandan et al. (2001) reported the anti-inflammatory activity of leaf and barks. Hence, the present study has been made to investigate the relaxant effect of macerated and soxhlet extracts of the *fruits* of *Syzygium cumini* and its possible mechanism(s) on guinea pig tracheal chains were examined.

MATERIALS AND METHODS

Plant and extracts:

Fruit of *Syzygium cumini* was collected from the chandaka jungle, Bhubaneswar. The Fruits of the plant was authenticated by Prof P K Sahu, Taxonomist, Botany Dept, Utkal University, Bhubaneswar. The soxhlet extract was prepared as follows: Fifty grams of the chopped, dried plant Fruits were extracted with 300 ml distilled water by suxhelat apparatus. For the preparation of the macerated extract, the same amount of plant was macerated with 300 ml distilled water (on a shaker) for 48 hr. The solvent of both extracts were then removed under reduced pressure at 50°C and distilled water were added to residues in such a way that plant ingredient concentration in the final soxhlet extracts were 10% W/W.

***Tissue Preparations*:**

Male guinea pigs (400-700g) were killed by a blow on the neck and tracheas were removed. Each trachea was cut into 10 rings (each containing 2-3 cartilaginous rings). The cartilages of all rings were then cut open opposite to the trachealis muscle, and sutured together to form a tracheal chain [14]. Tissue was then suspended in a 10 ml organ bath (Pinnacle Biomedical Research Institute(PBRI) Syamala Hills Bhopal (M.P.) India) containing Krebs-Henseliet solution of the following composition (mM): NaCl 120, $NaHCO_3$ 25, $MgSO_4$ 0.5, KH_2PO_4 1.2, KCl 4.72, $CaCl_2$ 2.5 and dextrose 11. The Krebs solution was kept at 37°C under stream of 95% O_2 and 5% CO_2 gases. Tissue was suspended under an isotonic tension of 1 g and allowed to equilibrate for at least 1 h while it was washed with Krebs solution every 15 min [16].

***Protocols*:**

The relaxant effects of four cumulative concentrations of macerated and soxhlet extracts (0.25, 0.5, 0.75, 1.0 and 1.25g/100 ml), four cumulative concentrations of theophylline anhydrous (S.D Fine, Mumbai,India) (0.25, 0.5, 0.75, 1.0and 1.25 mM) as positive control, and saline as negative control were examined. For preparation of different concentrations in the case of macerated and soxhlet extracts, 0.25 ml of 10% W/V of the concentrated extracts and in the case of theophylline, 0.25 ml of 10 mM solution were added to the organ bath. The consecutive volumes were added to organ bath at 5 min intervals. In each experiment the effect of four cumulative volumes of each extract, four cumulative volumes of theophylline, or saline on contracted tracheal smooth muscle were determined after exposure of tissue to the solution for 5 min. A decrease in tone was considered as a relaxant (broncho-dilatory) effect and expressed as positive percentage change in proportion to the maximum contraction and an increase in tone was consi-dered as a contractile (bronchoconstrictory) effect which was expressed as negative percentage change [15] [17].

The relaxant effect of different solutions ware tested with two different experimental designs as follows.

1. On tracheal chains contracted by 60 mM KCl (group 1experiments N = 6).
2. On non-incubated tracheal chains contracted by 10 µM methacholine hydrochloride (S.D Fine, India) (group 2 experiments N = 6).
3. On incubated tracheal chains with 1 µM propranolol hydrochloride 30 min prior to beginning and during the testing relaxation of different solutions. In this series of experiments, tracheal chains were also contracted by 10 µM methacholine hydrochloride (Group 3 experiments, N = 4).

The relaxant effect of theophylline was examined only on groups 1 and 2. The relaxant effects in three groups of experiments were examined in three different series of tracheal chains. All of the experiments were performed randomly with a 1 h resting period of tracheal chains between each two experiments while washing the tissues every 15 min with Krebs solution [16]. In all experiments responses were recorded on a kymograph and were measured after fixation.

Statistical analysis:

All data were expressed as mean ± SEM. Data of relaxant effects of different concentrations of extracts were compared with the results of negative and positive control using ANOVA. The data of relaxant effect obtained in three groups of experiments were also compared using ANOVA. The relaxant effect of two extracts and theophylline were related to the concentrations using least square regression. Significance was accepted at $P<0.05$.

RESULTS AND DISCUSSION

***Bronchodilator Effect*:**

In group 1 experiments only, the highest volumes of theophylline showed significant relaxant effects and soxhlet extract showed moderate relaxant effects compared to those of saline ($P < 0.05$ to $P < 0.001$). The effects of the last three concentrations of both extracts were significantly lower than those of theophylline ($P < 0.01$ to $P < 0.001$). In addition the effects of the last two concentrations of soxhlet extract were significantly higher than those of macerated extract in this group (**Table 1**). In groups 2 soxhlet extracts from *Syzygium cumini* and theophylline showed relatively potent and concentration-dependent relaxant effects on tracheal chains of guinea pig. The relaxant effects of the most concentrations of extracts and theophylline were significantly higher than those of saline ($P < 0.01$ to $P < 0.001$). Only the four concentration of macerated extract and three lower concentrations of soxhlet extract and two lower concentrations of theophylline did not show significant relaxant effects (**Table 2**). Only the two lower concentration of macerated extract and one lower concentrations of soxhlet extract did not show significant relaxant effects (**Table 3**). The relaxant effects of most concentrations of both extracts in group 2 and 3 were statistically greater than those of group 1 experiments ($P < 0.05$ to $P < 0.001$). The relaxant effect of most concentrations of both extract in group 3 were higher than those of group 2, There were significant positive correlations between the relaxant effects of both extracts and theophylline with concentrations of the solutions in all three experimental groups except that for macerated extract in group1 ($P < 0.05$ to $P < 0.001$) (**Table 4**). In addition, the effects of the different concentrations of soxhlet extract in this group were greater than those of macerated extracts, which were statistically significant ($p<0.05$), (**Table 1 & 2**).

Table No. 1: Relaxant effect of two different extracts from *syzygium cumini* in comparison with negative control (saline) and positive control (theophylline) in group 1 experiments (contracted tracheal chains with 60 mM KCl)

S. No.	Different Concentration	Saline	Macerated extract	Soxhlet extract	Theophylline
1	0.25	-	0.0 ± 0.0 NS, ns, nS	0.0 ± 0.0 NS, ns	1.70 ± 6.36 NS
2	0.5	-	0.0 ± 0.0 NS, ns, nS	3.93 ± 4.71 NS, ns	15.60 ± 2.16 NS
3	0.75	-	0.0 ± 0.0 NS, +++, nS	12.42 ± 2.28 NS, ++	41.40 ± 3.21***
4	1	-	6.58 ± 2.32 NS, +++,	41.35 ±11.80 *, +++	84.53 ± 5.15***
5	1.25	-1.47	9.85± 2.04 NS,	57.62 ± 11.43*	-

Note: Values are presented as mean ± SEM. Statistical differences between the effect of extracts and negative control (saline); NS: non-significant difference, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Statistical differences between the effect of extracts and positive control (theophylline); ns, non-significant difference, + $P < 0.05$, ++ $P < 0.01$, +++ $P < 0.001$. Statistical differences between the effect of two extracts; NS, non-significant difference; $P<0.05$; and $P<0.01$. The unit of concentration for extracts was w/v and for theophylline was mM.

Table No. 2: Relaxant effect of two dofferent extracts from *Syzygium cumini* in comparison with negative control (saline) and positive control (theophylline) in group 2 experiments (contracted tracheal chains by 10 µM methacoline)

S. No.	Different Concentration	Saline	Macerated extract	Soxhlet extract	Theophylline
1	0.25	-	5.25 ± 6.47 NS, ns	9.31 ± 5.80 NS, ns, nS	07.86 ± 3.43 NS
2	0.5	-	18.52 ± 14.24 NS, ns	29.59 ± 11.40*, ns, nS	22.87 ± 3.21 NS
3	0.75	-	25.28 ± 10.23***, ns	38.91±8.26***, ns, nS	54.27 ± 6.50*
4	1	-	35.64 ± 17.20***, ns	58.83 ± 6.08***, ns, nS	88.85 ± 6.87***
5	1.25	-1.40 ± 0.59	47.52 ± 12.60 NS,	70.62 ± 11.43*	-

Note: For abbreviations See Table I.

Table No. 3: Relaxant effect of two different extracts from *syzygium cumini* in comparison with negative control (saline) in group 3 experiments (incubated preparation with 1µM propranolol contracted tracheal chains by 10 µM methacholine)

S. No.	Different Concentration	Saline	Macerated extract	Soxhlet extract
1	0.25	_	22.47 ± 11.21	25.21 ± 12.41
2	0.5	_	39.36 ± 12.51**	46.23 ± 10.21**
3	0.75	_	51.23 ± 11.42***	60.44 ± 13.55***
4	1	_	65.27 ± 21.52***	76.57 ± 4.20***
5	1.25	-1.0 ± 0.21	74.25 ± 11.44***	92.70 ± 12.45***

Note: For abbreviations see Table I.

Table No. 4: Correlation(r) between the relaxant effects of two different extracts from *syzygium cumini* and theophylline with concentration in three groups of experiments

Different substances	Group 1	Group 2	Group 3
Soxhlet extract	0.651 ***	0.742 ***	0.934 ***
Macerated extract	0.321 NS	0.521 ***	0.674 ***
Theophy-lline	0.914 ***	0.932 ***	_

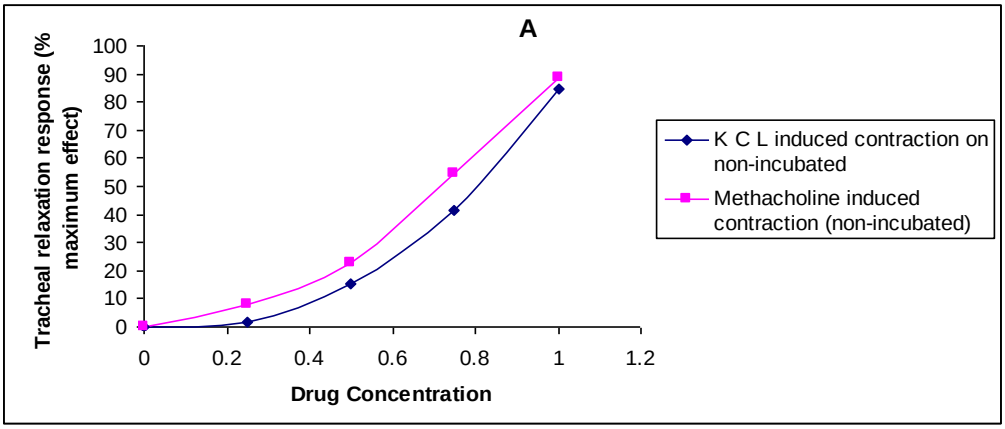

Fig. 1: Concentration response curves of the relaxant effects of theophylline (A)

Three different groups of experiments were as follows: group 1, kcl induced contraction on non-incubated tracheal chains (o n = 6); group 2, methacholine induced contraction on non-incubated tracheal chains (n = 6), and group 3, methacholine-induced contraction on incubated tracheal chains of guinea pig with propranolol (♦ n = 4). statistical differences in the relaxant effect of different substances between group 1 with those of group 2 and 3; ns, non-significant difference; * $p < 0.05$; ** $p < 0.01$; and *** $p < 0.002$. statistical differences in the relaxant effect of different substances between groups 2 and 3; ns, non-significant difference; + $p < 0.05$; and ++ $p < 0.01$.

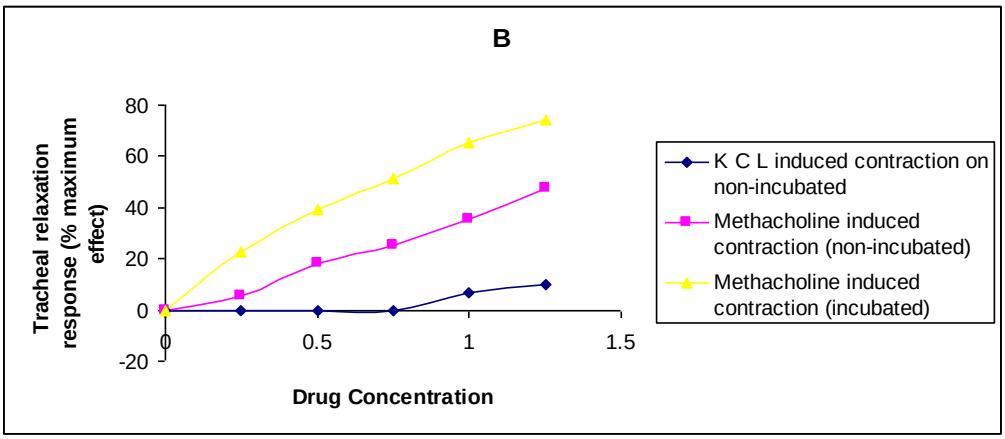

Fig. 2: Concentration response curves of the relaxant effects of macerated extract (B)

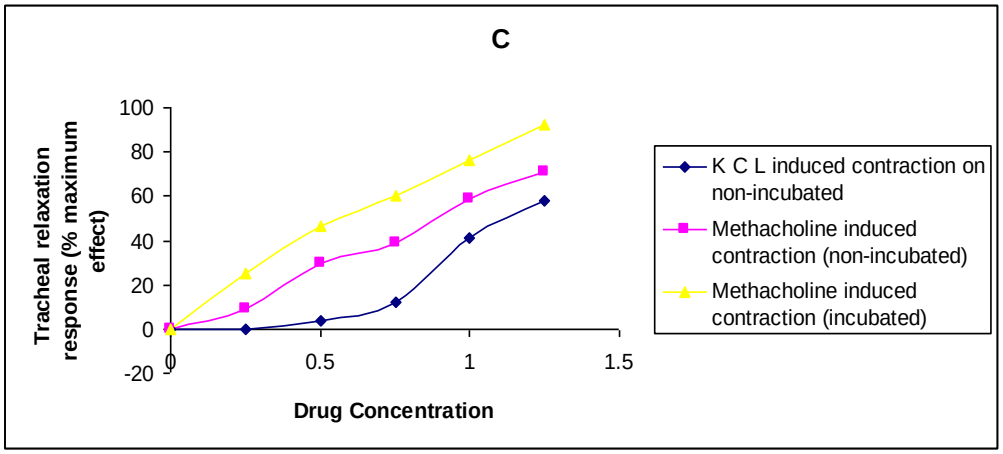

Fig. 3: Concentration response curves of the relaxant effects of soxhlet extract (C)

CONCLUSION

The study indicates that the relaxant (bronchodilatory) effects of soxhlet and macerated extract from *Syzygium cumini* in comparison with saline as negative control and theophylline as positive control were studied. In group 1 experiments (contracted tracheal chains by KCl) only the highest concentrations of theophylline and highest two concentration of soxhlet extract showed relaxant effect. The macerated extract and saline did not show any relaxant effect in this group of experiments. However, soxhlet extracts from *Syzygium cumini* showed relatively potent relaxant effects compared with the effect of saline in groups 2 and both extracts from 3 experiments. The effects of all concentrations of soxhlet and macerated extract in groups 2 and 3 were comparable with those of theophylline in group 2. However, the effect of theophylline was not examined in group 3 experiments. The relaxant effect of different extracts from *Syzygium cumini* on tracheal chains of guinea pigs might be produced due to several different mechanisms including stimulation of β-adrenergic receptors [21], inhibition of histamine H1 receptors [22]. The relaxant effects of most concentrations of both extracts from *Syzygium cumini* obtained in the group 3 experiments were non-significantly greater than those of group 2. The relaxant effect of both extracts and theophylline was concentration dependent. There were positive correlations between increasing the concentrations of the soxhlet extracts and the relaxant effects in all three experimental groups. The absence of obvious relaxant effect of macerated extract from *Syzygium cumini* in group 1 and the relatively potent relaxant effect of this extract in group 2 and 3 experiments may indicate an opening effect of these fractions on potassium channels because the bronchodilatory effect of potassium channel opening has been demonstrated previously [21]. If the aqueous extract had a potassium channel opening effect, they would not have relaxant effect on tracheal chains contracted by KCl, while they could show relaxant effect when the tracheal chain was contracted by metacholine, While KCl affect calcium channels [22] and with regard of bronchodilatory effect of calcium channel blockers [23] [24] another explanation for these findings is the absence of a blocking effect of this extract on calcium channels. However, the significant relaxant effect of soxhlet extract in group 1 experiment may suggest the absence of any effect on potassium channels and/or a calcium channels blocking effect for this extract. The effects of different concentrations of soxhlet extract in both groups of experiments were greater than those of macerated extract. This may suggest that the effective substances in soxhlet extract are higher than that of macerated extract. The other possible mechanisms for broncho-dilatory effect include: stimulation of β-adrenergic receptors [18], blocking of histamine H1 receptors [19], anticholinergic activity [20]. However, contributions of these mechanisms to bronchodilatory effect of extracts of *Syzygium cumini* on tracheal chains of guinea pigs (s) should be clarified in further studies. In addition *Syzygium cumini* might also have an anti-inflammatory effect, which will contribute to the therapeutic effect of this plant on asthma. While anti-inflammatory [25] and anti-oxidant [26] effects of this plant have been reported, the effect of, *Syzygium cumini* on airway inflammation which is present in asthma should be investigated in further studies.

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REFERENCES:

1. P. Warrier, V. Nambiar and C. Ramankutty. "Indian Medical Plants", Orient Longman Ltd: Hyderabad, India, **1996**: 5; pp 225-228.
2. H. Sagrawat, A. Mann and M. Kharya. "Pharmacological potential of Eugenia jambolana: a review," Pharmacoge-nesis Magazice, **2006**: 2; pp 96-104
3. Chopra, R.Nayar, S. Chopra, I. Glossary of Indian medicinal plant, 3 Edn. Council of Scientific and Industrial Research. New Delhi, **1986**; 249.
4. http://rarefruit.hypermart.net/Exotic1.html. **2005**: pp 1-2.
5. Muruganandan S, Srinivasan K, Chandra S, Tandan SK, Lal J, Raviprakash V. Anti- inflammatory activity of Syzygium cumini leaves. Fitoterapia., **2001**: 72; pp 369-375.
6. Kim HM, Lee EH, Hong SH, Song HJ, Shin MK, Kim SH, et al. Effect of Syzygium aromaticum extract on immediate hypersensitivity in rats. *J. Ethnopharmacol.,* **1998**: 60; pp 125-131.
7. Muruganandan S, Pant S, Srinivasan K, Chandra S, Tandan SK, Lal J, et al. Inhibitory role of Syzygium cuminion autacoid-induced inflammation in rats. *Indian J. Physiol. Pharmacol.,* **2002**: 46; pp 482-486.
8. Shakoory B, Fitzgerald SM, Lee SA, Chi DS, Krishnaswamy G. The role of human mast cell-derived cytokines in eosinophil biology. *J. Interferon Cytokine Res.,* **2004**: 24; pp 271-281.
9. Smith, A.C. Flora Vitiensis nova, A new flora of Fiji, National Tropical Botanical Garden. **1991**; P5.
10. Vuillaume, M. Mut. Res., **1987**: 186; pp 43-72.
11. Meneghine, R. Mut. Res., **1988**: 195; pp 215-230.
12. Ndubani, P. and Hojer, *B. J. Ethnopharmacol.,* **1999**: 67; pp 15-25.
13. http://www.stuartxchange.org/Duhat.html.
14. Holroyde MC. The influence of epithelium on the responsiveness of guinea-pig isolated trachea. *Br. J. Pharmacol*., **1986**: 87; pp 501-507.
15. Martin CAE, Naline E, Bakdach H, Advenier C. Beta3 adrenoceptor agonists, BRL 37344 and SR 58611A do not induce relaxation of human, sheep and guinea-pig airway smooth muscle in vitro. *Eur. Respir. J.,* **1994**: 7; pp 1610-1615.
16. Mohammad Hossein Boskabady, Sahar Kiani, Behnia Haghiri. Relaxant effects of ocimum basilicum on guinea pig Tracheal chains and its possible mechanism(s). *http://journals.tums.ac.ir/.,* **2005**: 13; pp 28-33.
17. Boskabady MH., Aslani MR., Mansuri F. Amery S. Relaxant effect of Satureja hortensis on guinea pig tracheal chains and its possible mechanism(s). *http://journals.tums.ac.ir/.* **2007**: 15; pp 199-204.
18. Linden A, Bergendal A, Ullman A, Skoogh BE, Lofdahl CG. Salmetrol, formetrol, and salbutamol in the isolated guinea-pig trachea: differences in maximum relaxant effect and potency but not in functional antagonism. Thorax. **1993**: 48; pp 547-553.
19. Popa VT, Somani P, Simon P, Simon V. The effect of inhaled verapamil on resting bronchial tone and airway constriction by histamine and acetylcholine in normal and asthmatic subjects. Am. Rev. Respir. Dis., **1984**: 130; pp 106-113.
20. Lronards B, Rampart M, Herman AG. Selective M3 muscarinic receptor inhibit smooth muscle contraction in rabit trachea without increasing the release of acetylcholine. *J. Pharmacol. Exp. Ther.,* **1992**: 263; pp 773-770.

21. Buckle DR, Arch JRS, Boering NE, Foster KA, Taylor JF, Taylor SG, Shaw DJ. Relaxation effect of potassium channel activators BRL 38227 and Pinacidil on guinea-pig and human airway smooth muscle, and blockade of their effects by Glibenclamide and BRL 31660. *Pulmon. Pharmacol.,* **1993**: 6; pp 77-86.
22. Perez-Guerrero C, Suarez, J, Herrera MD, Marhuenda E. Spasmolytic effect of tetrazepam on rat duodenum and guinea pig ileum. *Pharmacol. Res.,* **1997**: 35; pp 493-494.
23. Miyahara Y, Kizawa Y, Sano M, Murakami H. Effect of organic and inorganic Ca 2+antagonists on acetylcholine induced contraction in molluscan (Mytilus edulis) smooth muscle. *Gen. Pharmacol.,* **1993**: 24; pp 1419-1423.
24. McCaig D, DeJonckeere S. Effect of two Ca2+modulator in normal and albumin sensitised guinea pig trachea. *Eur. J. Pharmacol.,* **1993**: 249; pp 53-63.
25. Shobha Borhade. Antibacterial Activity, phytochemical Analysis of Water Extract of Syzygium Cumini And Analytical Study By HPLC. *Asian J. Exp. Biol. Sci*., **2012**: 3(2); pp 320-324.
26. F.A. Brito, L.A. Lima, M.F.S. Ramos, M.J. Nakamura, S.C. Cavalher-Machado, A.C. Siani, M.G.M.O. Henriques and A.L.F. Sampaio. Pharmacological study of anti-allergic activity of Syzygium cumini (L.) Skeels. *Brazilian Journal of Medical and Biological Research,* **2007**: 40; pp 105-115.

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