March 2008

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Mechanisms underlying the antispasmodic and bronchodilatory properties of *Terminalia bellerica* fruit

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Received 21 September 2007; received in revised form 17 December 2007; accepted 4 January 2008

Available online 16 January 2008

Abstract

**Aim of the study:** The present investigation was carried out to provide the pharmacological basis for the medicinal use of *Terminalia bellerica* in hyperactive gastrointestinal and respiratory disorders.

**Materials and methods:** Crude extract of *Terminalia bellerica* fruit (Tb.Cr) was studied in *in vitro* and *in vivo*.

**Results:** Tb.Cr caused relaxation of spontaneous contractions in isolated rabbit jejunum at 0.1–3.0 mg/mL. Tb.Cr inhibited the carbachol (CCh, 1 \( \mu \)M) and K\(^+\) (80 mM)-induced contractions in a pattern similar to that of dicyclomine, but different from nifedipine and atropine. Tb.Cr shifted the Ca\(^+\+) concentration–response curves to right, like nifedipine and dicyclomine. In guinea-pig ileum, Tb.Cr produced rightward parallel shift of acetylcholine-curves, followed by non-parallel shift at higher concentration with the suppression of maximum response, similar to dicyclomine, but different from nifedipine and atropine. Tb.Cr exhibited protective effect against castor oil-induced diarrhea and carbachol-mediated bronchoconstriction in rodents. In guinea-pig trachea, Tb.Cr relaxed the CCh-induced contractions, shifted CCh-curves to right and inhibited the contractions of K\(^+\). Anticholinergic effect was distributed both in organic and aqueous fractions, while CCB was present in the aqueous fraction.

**Conclusions:** These results indicate that *Terminalia bellerica* fruit possess a combination of anticholinergic and Ca\(^+\+) antagonist effects, which explain its folkloric use in the colic, diarrhea and asthma.

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**Keywords:** *Terminalia bellerica* fruit; Anticholinergic; Ca\(^+\+) antagonist; Gastrointestinal and respiratory disorders

1. Introduction

*Terminalia bellerica* Roxb. (family: Combretaceae) commonly known as “belleric myrobalan” and locally as “bahera” is a large deciduous tree, found throughout Central Asia and some other parts of the world (Kapoor, 1990). Its fruit is used in folk medicine to treat anemia, asthma, cancer, colic, cough, diarrhea, dyspepsia, dysuria, headache, hoarseness, hypertension, inflammations and rheumatism. The half ripe fruit is considered purgative. It is one of the constituent of “Triphala” which is prescribed in the diseases of the liver and gastrointestinal tract (Usmanghani et al., 1997; Duke et al., 2002).

The plant is reported to contain termilignan, thannilignan, 7-hydroxy-3',4'-(methylenedioxy) flavone and anolignan B (Valsaraj et al., 1997), gallic acid, ellagic acid, \( \beta \)-sitosterol (Anand et al., 1997), arjungenin, belleric acid, bellericoside (Nandy et al., 1989) and cannogenol 3-O-\( \beta \)-d-galactopyranosyl-(1 → 4)-O-\( \alpha \)-l-rhamnopyranoside (Yadava and Rathore, 2001).

*Terminalia bellerica* is scientifically proven to possess antioxidant activity (Saleem et al., 2001). The plant is known to lower the levels of lipid in hypercholesterolemic animals (Thakur et al., 1988; Shaila et al., 1995). It was found effective against several pathogens including *Bacillus subtilis*, *Proteus vulgaris*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* (Ahmad et al., 1998). It exhibited inhibitory effect on human immunodeficiency virus-1 reverse transcriptase (El-Mekkawy et al., 1995). *Terminalia bellerica* reduced the serum glucose level both in normal and alloxan-induced diabetic rats (Sabu and Kuttan, 2002).

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and also showed preventive effect against the myocardial necrosis in rats (Tariq et al., 1977). Dwivedi et al. (1994), Srivastava et al. (1992) and Khan and Gilani (in press) reported that Terminalia bellerica lowers the arterial blood pressure. A water soluble fraction obtained from the defatted fruits of Terminalia bellerica caused protection against CCl₄-induced liver injury in rodents (Anand et al., 1994). In a clinical study, Terminalia bellerica was found to possess antispasmodic, antiasthmatic and antitussive effects (Trivedi et al., 1979). A polyherbal formulation containing Terminalia bellerica exhibited antimutagenic activity (Kaur et al., 2002).

We have experienced that plants with medicinal use in hyperactive gut and airways disorders usually exhibit spasmylic effect through combination of mechanisms (Gilani et al., 2005a,b, 2008). In this investigation, we report the presence of a combination of anticholinergic and Ca++ antagonist effects in the Terminalia bellerica, which justify its medicinal use in such conditions.

2. Materials and methods

2.1. Plant material, preparation of crude extract and fractions

The fruits of Terminalia bellerica were bought from a local market in Dhaka (Bangladesh) and was authenticated by Assistant Professor, Mehboob-ur-Rehman, Department of Botany, Govt. Postgraduate Jehanzeb College, Saidu Sharif, Swat, N.W.F.P., Pakistan. A sample voucher (TB-FR-10-95-30) was submitted to the herbarium of Department of Biological and Biomedical Sciences, Aga Khan University, Karachi. After cleaning of adulterant material, 432 g of fruits were crushed and soaked in 3 L of 70% aqueous-methanol for three days with occasional shaking. It was filtered through a muslin cloth and then through a Whatman qualitative grade 1 filter paper (Williamson et al., 1998). This procedure was repeated thrice and the combined filtrate was evaporated on rotary evaporator to obtain the crude extract (Tb.Cr), yielding approximately 9.25%.

Activity-guided fractionation was carried out by using solvents of increasing polarity to obtain organic and aqueous fractions. Tb.Cr was dissolved in about 150 mL of distilled water. The chloroform was added to it with vigorous shaking. The chloroform layers (lower) were collected thrice and evaporated on rotary evaporator to give the chloroform fraction (Tb.CHCl₃). The other layer (upper) was again taken into a separating funnel, ethyl acetate was added into it, separated and was also evaporated in rotary evaporator to give the ethyl acetate fraction (Tb.EtAc). The remaining lower layer was collected and evaporated to obtain the aqueous fraction (Tb.Aq).

2.2. Drugs and animals

Acetylcholine (ACh), atropine, carbachol (CCh), dicyclomine, loperamide and nifedipine were purchased from Sigma Chemicals Co., St. Louis, MO, USA. Salbutamol, pentothal sodium (thiopental sodium) and castor oil were respectively obtained from Glaxo Wellcome, Abbot Laboratories and KCL Pharma, Karachi, Pakistan. Chemicals used for making physiological salt solutions were potassium chloride (Sigma Chemicals Co.), calcium chloride, glucose, magnesium chloride, magnesium sulfate, potassium dihydrogen phosphate, sodium bicarbonate, sodium dihydrogen phosphate (Merck, Darmstadt, Germany) and sodium chloride from BDH Laboratory Supplies, Poole, England. All chemicals used were of the analytical grade available and solubilized in distilled water.

Animals used in this study such as Chinchilla rabbits (1–1.2 kg), Himalayan guinea-pigs (500–550 g), Sprague–Dawley rats (200–250 g) and Balb-C mice (20–25 g) of either sex were housed at the Animal House of the Aga Khan University, maintained at 23–25°C. Animals were given tap water ad libitum and a standard diet. Rabbits and guinea-pigs had free access to water, but food was withdrawn 24 h prior to experiment and sacrificed by blow on back of the head.

Experiments performed complied with the rulings of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (1996) and approved by the Ethical Committee of the Aga Khan University.

2.3. Isolated tissue preparations

2.3.1. Rabbit jejunum

The jejunum was dissected out, kept in Tyrode’s solution and cleaned of mesenteries (Ghayur and Gilani, 2005). Each segment of about 2 cm length was suspended in a 10 mL tissue bath containing Tyrode’s solution, maintained at 37°C and aerated with a mixture of 95% oxygen and 5% carbon dioxide (carbogen). The composition of the Tyrode’s solution in mM was KCl 2.68, NaCl 136.9, MgCl₂ 1.05, NaHCO₃ 11.90, NaH₂PO₄ 0.42, CaCl₂ 1.8 and glucose 5.55. Intestinal responses were recorded isotonically using Bioscience transducers and oscillograph. Each tissue was allowed to equilibrate for at least 30 min before the addition of any drug and then stabilized with a sub-maximal concentration of ACh (0.3 μM) with a 3 min interval in between until constant responses were recorded. Under these experimental conditions, rabbit jejunum exhibits spontaneous rhythmic contractions, allowing the testing of relaxant (spasmolytic) activity directly without the use of an agonist.

For the determination of Ca++ channel blocking (CCB) activity, high K+ (80 mM) was used to depolarize the preparations as described by Farre et al. (1991). High K+ (>30 mM) is known to cause smooth muscle contractions through opening of voltage-dependent L-type Ca++ channels, thus allowing influx of extracellular Ca++ causing a contractile effect (Bolton, 1979) and a substance causing inhibition of high K+-induced contraction is considered as a blocker of Ca++ influx (Godfraind et al., 1986). To elucidate the presence of any additional spasmolytic effect, the plant extract was tested on CCh-induced contractions. CCh is a cholinergic agonist which causes smooth muscle contraction through activation of muscarinic receptors (Jenkinson, 1963).
2.4. In vivo experiments

2.4.1. Castor oil-induced diarrhea

Mice were fasted for 24 h before the experiment (Borelli et al., 2006). The animals were housed in individual cages and divided in four equal groups. The first group received saline as the vehicle control (10 mL/kg, p.o.) and so acted as the negative control. The dose of the crude extract was selected on a trial basis and then two increasing doses of the crude extract were given to the two different group animals. A fourth group of mice was treated with loperamide (10 mg/kg, p.o.), as the positive control. One hour after the treatment, each animal received 10 mL/kg of castor oil orally through a feeding needle. Afterwards, the cages were inspected for the presence of the typical diarrheal droppings; their absence was noted as a positive result, indicating protection from diarrhea at that time.

2.4.2. Bronchodilatory activity

Rats were anaesthetized with sodium thiopental (80–100 mg/kg, i.p.), then incubated with a tracheal tube and ventilated with a volume ventilator (Miniature ideal pump, Bioscience, UK) adjusted at a rate of 70–80 strokes/min (to deliver 7–10 mL/kg of room air) in the supine position (Channa et al., 2005). A polyethylene catheter was inserted into the jugular vein for drugs administration. Changes in airways resistance was measured by connecting to a side arm of tracheal cannula a pressure transducer (MLT1199) and recorded by a PowerLab 4/25 via bridge amplifier (Quad Bridge Amp, ML112) running Chart software, ver. 5.5 (ADInstruments, Bella Vista, NSW, Australia). Bronchoconstriction was induced with carbachol (CCh 1 μM/kg), which was reversed within 7–10 min. The test drug was given to the animals 5–8 min prior to administration of CCh. The responses were expressed as the per cent reduction of the CCh-induced bronchospasm.

2.4.3. Acute toxicity test

Animals were divided in groups of five mice each. The test was performed using increasing doses of the plant extract, given orally, in 10 mL/kg volume to different groups serving as test groups (Sanmugapriya and Venkataraman, 2006). Another group of mice was administered saline (10 mL/kg, p.o.) as negative control. The mice were allowed food ad libitum and kept under regular observation for 6 h while the lethality was recorded after 24 h.

2.5. Statistical analysis

All the data expressed are mean ± standard error of mean (S.E.M., n = number of experiments). Inhibitory effects are expressed as the median inhibitory concentrations (IC50), while
effects of the contractile agents as maximum effective concentrations ($E_{\text{max}}$) and median effective concentrations (EC$_{50}$) with 95% confidence intervals (CI). CRCs were analyzed by non-linear regression using GraphPad3 program (GraphPAD, San Diego, CA, USA). The statistical parameter applied is Student’s $t$-test except in the antidiarrheal study where Chi-square test was used. $P<0.05$ was considered significantly different.

3. Results

3.1. Effect of Tb.Cr on rabbit jejunum

Tb.Cr, dicyclomine, nifedipine and atropine caused relaxation of rabbit jejunum spontaneous contractions with the respective IC$_{50}$ values of 1.2 mg/mL (0.9–1.7, 95% CI, $n = 5$), 0.6 µM (0.42–0.8, $n = 4$), 0.15 µM (0.10–0.22, $n = 4$) and 0.006 µM (0.002–0.01, $n = 4$) as shown in Fig. 1. When tested against CCh (1 µM) and K$^+$ (80 mM)-induced contractions, Tb.Cr was found (Fig. 2A) to inhibit the CCh-induced contractions at lower concentration with IC$_{50}$ value of 1.05 mg/mL (0.6–1.8, $n = 4$) as compared to its effect against K$^+$ with IC$_{50}$ value of 8.1 mg/mL (4.7–14.1, $n = 4$). Dicyclomine, also showed a similar pattern of inhibitory effect (Fig. 2B) with respective IC$_{50}$ values of 0.21 (0.14–0.31, $n = 6$) and 2.9 µM (1.9–4.7, $n = 6$), whereas nifedipine was more potent against K$^+$-induced contractions with IC$_{50}$ value of 0.02 µM (0.015–0.03, $n = 5$), when compared with CCh-induced contractions [0.20 µM (0.12–0.29, $n = 5$)] as shown in Fig. 2C. Atropine relaxed the CCh (1 µM)-induced contraction potently with IC$_{50}$ value of 0.0025 µM (0.002–0.004, $n = 8$), without any effect on K$^+$ (80 mM)-induced contractions, $n = 8$ (Fig. 2D), as expected. When tested for the possible interaction with Ca$^{++}$ channels, Tb.Cr produced rightward shift in the Ca$^{++}$ CRCs (Fig. 3A), similar to that caused by nifedipine (Fig. 3B) and dicyclomine (Fig. 3C). Respective $E_{\text{max}}$ values of Ca$^{++}$ CRCs in the absence and presence of Tb.Cr, nifedipine and dicyclomine are given in Table 1.
3.2. Effect of Tb.Cr on guinea-pig ileum

Tb.Cr at 1.0 mg/mL caused a rightward parallel shift in the ACh-curves without suppression of maximum contractile response, followed by non-parallel shift with the suppression of maximum response at 3.0 mg/mL (Fig. 4A). Dicyclomine (0.03–0.1 μM) also showed a similar pattern of shift (Fig. 4B), while nifedipine (0.03–0.1 μM) produced a non-parallel rightward shift with the suppression of the maximum response (Fig. 4C). Atropine (0.01–0.03 μM) caused rightward parallel...
Table 1
The maximum effective concentrations ($E_{\text{max}}$) and median effective concentrations (EC$_{50}$) values of the Ca$^{++}$, acetylcholine (ACh) and carbachol concentration–response curves in the absence (Control) and presence of different concentrations (Conc.) of the crude extract of Terminalia bellerica fruit (Tb.Cr), dicyclomine, nifedipine and atropine.

<table>
<thead>
<tr>
<th>Test drugs</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ca$^{++}$</td>
</tr>
<tr>
<td></td>
<td>Control: 100%</td>
</tr>
<tr>
<td>Tb.Cr (mg/mL)</td>
<td>3</td>
</tr>
<tr>
<td>Conc.</td>
<td>5</td>
</tr>
<tr>
<td>Dicyclomine (μM)</td>
<td>Control: 100%</td>
</tr>
<tr>
<td>Conc.</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Nifedipine (μM)</td>
<td>Control: 100%</td>
</tr>
<tr>
<td>Conc.</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
</tr>
<tr>
<td>Atropine (μM)</td>
<td>Control: 0.25 μM (0.17-0.37)</td>
</tr>
<tr>
<td>Conc.</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>0.03</td>
</tr>
</tbody>
</table>

The values given with percentage (%) represent $E_{\text{max}}$ and those with μM are EC$_{50}$. Values represent geometric means along with 95% confidence intervals in parenthesis. ** $P<0.01$, *** $P<0.001$ vs. respective control, Student’s t-test.

Table 2
Effect of the crude extract of Terminalia bellerica fruit (Tb.Cr) on castor oil (C. oil, 10 mL/kg)-induced diarrhea

<table>
<thead>
<tr>
<th>Treatment (p.o.)</th>
<th>No. of mice/5 with diarrhea</th>
<th>% Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline (10 mL/kg)+ C. oil</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Tb.Cr (300 mg/kg)+ C. oil</td>
<td>4</td>
<td>20</td>
</tr>
<tr>
<td>Tb.Cr (1000 mg/kg)+ C. oil</td>
<td>2a</td>
<td>60</td>
</tr>
<tr>
<td>Loperamide (10 mg/kg)+ C. oil</td>
<td>1a</td>
<td>80</td>
</tr>
</tbody>
</table>

a $P<0.05$ vs. saline group, Chi-square test.

shift without the suppression of the maximum contractile effect (Fig. 4D). Table 1 shows respective $E_{\text{max}}$ and EC$_{50}$ values of ACh in the absence and presence of Tb.Cr, dicyclomine, nifedipine and atropine.

3.3. Effect of Tb.Cr on castor oil-induced diarrhea in mice

Tb.Cr exhibited a dose-dependent (300–1000 mg/kg) protective effect against castor oil-induced diarrhea in mice. The negative control group (saline treated) did not show any protection against castor oil-induced diarrhea. Pretreatment of animals with the plant extract, showed 20% protection from diarrhea at 300 mg/kg dose and 60% protection at 1000 mg/kg ($P<0.05$ versus saline group). Loperamide (10 mg/kg) showed 80% protection from diarrhea in the positive control group (Table 2).

3.4. Effect of Tb.Cr on carbachol-induced bronchoconstriction in rats

Tb.Cr at the doses of 30, 100 and 300 mg/kg produced 18 ± 2.8, 39.4 ± 4.05 and 97.6 ± 0.81% (n = 5) respective inhibition of CCh (1 μM/kg)-induced increase in inspiratory pressure in anaesthetized rats (Fig. 5A). Salbutamol was used as a positive control which caused suppression of CCh-induced bronchoconstriction at 0.01, 0.03 and 0.1 mg/kg by 22.75 ± 1.31, 42.5 ± 3.2 and 69.35 ± 1.03% (n = 4), respectively (Fig. 5B).

3.5. Effect of Tb.Cr on guinea-pig trachea

In tracheal preparations, Tb.Cr caused inhibition of CCh (1 μM)-induced contractions at low concentrations with IC$_{50}$ value of 3.3 mg/mL (1.7–6.7, n = 4) compared to that against K$^+$ (80 mM)-induced contractions with IC$_{50}$ value of 8.5 mg/mL.
Fig. 5. Effect of increasing doses of (A) crude extract of <em>Terminalia bellerica</em> fruit (Tb.Cr) and (B) salbutamol on carbachol-mediated bronchoconstriction in anaesthetized rats. Results are expressed as mean ± S.E.M., n = 4–5.

(2.4–30.5, n = 4) as shown in Fig. 6A. Dicyclomine, also showed a similar pattern of inhibitory effect (Fig. 6B) with respective IC<sub>50</sub> values of 0.3 (0.20–0.41, n = 4) and 4.24 μM (2.5–7.1, n = 4), whereas nifedipine was more potent against K<sup>+</sup>-induced contractions with IC<sub>50</sub> value of 0.03 μM (0.02–0.05, n = 4), when compared with CCh-induced contractions [0.33 μM (0.24–0.50, n = 4)] as shown in Fig. 6C. Atropine relaxed the CCh (1 μM)-induced contraction potently with IC<sub>50</sub> value of 0.003 μM (0.002–0.005, n = 4), without any effect on K<sup>+</sup> (80 mM), while Tb.Aq relaxed both CCh and K<sup>+</sup> (80 mM)-induced contractions (being more potent against CCh) with respective IC<sub>50</sub> values of 0.21 (0.15–0.3, n = 4) and 7.7 mg/mL (3.9–15.3, n = 5) as shown in Fig. 8.

4. Discussion

Due to the folkloric reputation of <em>Terminalia bellerica</em> as a gastrointestinal relaxant, its fruit extract was tested for its possible spasmytic effect in spontaneously contracting rabbit jejunum preparations, where it inhibited spontaneous contractions, thus showing an antispasmodic action.

To assess the possible mechanisms of spasmytic effect, the extract was tested on the induced contractions. Tb.Cr reversed the CCh and K<sup>+</sup>-induced contractions, being more potent against CCh. Dicylomine, a dual blocker of muscarinic receptors and Ca++ influx (McGrath et al., 1964; Downie et al., 1977) showed similar pattern of inhibition, while nifedipine, a standard Ca ++ channel blocker (Fleckenstein, 1977) was more potent against the induced contractions of K+ than CCh and atropine, a muscarinic receptor antagonist (Arunlakhshana and Schild, 1959) relaxed the CCh-induced contractions only. It is thereby suggested that the inhibitory effect of the plant extract is mediated possibly through a combined blockade of Ca++ influx and muscarinic receptors.

The presence of dual mode of inhibition, involving Ca++ antagonist and anticholinergic was confirmed through constructing the Ca++ and ACh CRCs in the presence of different concentrations of the extract. In jejunum, Tb.Cr shifted the Ca++ curves to the right accompanied by the suppression of maximum response, similar to that caused by nifedipine and dicyclomine. The anticholinergic activity was evaluated by acetylcholine-concentration–response curves constructed in guinea-pig ileum. A parallel displacement of ACh-curves without suppression of the maximum effect was observed at the lower concentration, a characteristic of a competitive or specific antagonist, like atropine (Gilani and Cobbin, 1986; Eglen and Harris, 1993), followed by non-parallel shift with suppression of the maximum response, similar to that caused by nifedipine and dicyclomine. The anticholinergic activity was evaluated by acetylcholine-concentration–response curves constructed in guinea-pig ileum. 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Dicyclomine also shifted the ACh-curves to the right, similar to that of the crude extract, while nifedipine resulted in a parallel shift with suppression of the maximum effect at both the...
Fig. 6. Concentration–response curves showing comparison of (A) crude extract of *Terminalia bellerica* fruit (Tb.Cr), (B) dicyclomine, (C) nifedipine and (D) atropine for the inhibitory effect against carbachol and K⁺-induced contractions in isolated guinea-pig tracheal preparations. Results are expressed as mean ± S.E.M., n = 4.

Fig. 7. Concentration–response curves of carbachol in the absence and presence of (A) crude extract of *Terminalia bellerica* fruit (Tb.Cr), (B) dicyclomine, (C) nifedipine and (D) atropine in isolated guinea-pig tracheal preparations. Results are expressed as mean ± S.E.M., n = 3–5.
concentrations used. Atropine caused a rightward parallel shift of the ACh-curves without suppression of maximum response.

The in vivo antidiarrheal property of *Terminalia bellerica* fruit was determined by its protective effect against castor oil-induced diarrhea in mice. The induction of diarrhea with castor oil results from the action of ricinoleic acid formed in the hydrolysis of the oil (Iwao and Terada, 1962) which produces changes in the transport of electrolytes and water resulting in the generation of giant contractions of the transverse and distal colon (Izzo et al., 1994; Croci et al., 1997). Thus, a potential antidiarrheal agent may exhibit its effect by inhibiting bowel contractions (Di-Carlo et al., 1993). The effect of Tb.Cr was in accordance with the expectation, as both anticholinergic drugs and Ca++ antagonists were reported to possess an antidiarrheal action (Reynolds et al., 1984; Rang et al., 1999).

Based on the use of *Terminalia bellerica* in hyperactive respiratory ailments, the plant extract was evaluated for bronchodilatory effect in rats under anesthesia. The extract protected the CCh-evoked bronchospasm in a dose-dependent fashion. Tb.Cr was then studied in isolated trachea to investigate the possible mode of bronchodilatory action. Similar to the gut, the crude extract caused inhibition of CCh-induced contractions and displaced the CCh-curves to the right in a parallel fashion without suppression of the maximum response at low concentration, followed by non-parallel shift with suppression of the maximum effect at the next higher concentration. Tb.Cr also relaxed the K+-induced contractions at higher concentration, suggesting the co-existence of anticholinergic and Ca++ antagonist properties, like dicyclomine. Nifedipine was more potent against K+ than CCh-induced contractions and caused a rightward non-parallel shift of CCh-curves with suppression of the maximum effect. Atropine inhibited the CCh-induced contractions, without any effect on K+ and caused a rightward parallel shift of CCh-curves without suppression of maximum response. Both the crude extract and dicyclomine were slightly more effective in the gut preparations than in the trachea. This could possibly be due to difference in the physiological modulators among various tissues and/or the extent of their regulatory influences (Gayton and Hall, 1996) may cause a better synergistic interaction of the different spasmolytic mechanisms in the gut compare to airways, though species difference cannot be ruled out.

The study on the activity-directed fractionation revealed that the Ca++ antagonist component was concentrated in the aqueous fraction, while anticholinergic agent was distributed both in organic and aqueous fractions, with the ethyl acetate fraction exhibiting the most potent in its antispasmodic effect.

5. Conclusions

These results show that *Terminalia bellerica* offers a combination of anticholinergic and Ca++ antagonist properties, which provide pharmacological basis for its usefulness in the hyperactive gastrointestinal and respiratory disorders. Moreover, this study by reporting the in vivo antidiarrheal and bronchodilatory effects of *Terminalia bellerica* fruit contributes towards evidence-based phytomedicine.

Acknowledgement

This study was supported by funds made available by the Higher Education Commission of Pakistan under the scheme of Distinguished National Professor Research Allowance.
References


