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Original Research Article

Anti-inflammatory and analgesic properties of *Caesalpinia bonducella* leaf aqua in animals

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ABSTRACT

Background: The medicinal plant *Caesalpinia bonducella* (CBC; Karanjwa) is widely spread in India's coastal region, Burma, Sri Lanka, and other tropical and subtropical regions of the world. The goal of this study was to see if *Caesalpinia bonducella* had analgesic and anti-inflammatory properties in laboratory animals.

Materials and Methods: Acetic acid-induced abdominal writhing and a hot plate test were used to assess analgesic efficacy in rats at doses of 7, 10.50, and 14 mg/kg. Carrageenan was used to assess anti-inflammatory properties in rats.

Results: There was a significant reduction in the number of writhing in 20 minutes observed. There was a significant increase in the reaction time observed for 30 min, 60 min, and 90 min. A significant reduction in the paw volume was observed at Ist, 3rd, and 5th hr.

Conclusion: *Caesalpinia bonducella* was found to have strong analgesic and anti-inflammatory action in rats, according to the findings.

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INTRODUCTION

The use of plants, plant extracts, or plant-derived pure chemicals to treat disease has become a time-tested therapeutic modality. According to the World Health Organization (WHO), traditional remedies (primarily herbs) are used by about three-quarters of the world's population for health care. Traditional remedies, sometimes known as an herbal or natural medicine for a time, existed in one form or another in various cultures/civilizations, including Egyptians, Westerners, Chinese, Kampo (Japan), and Greco-Arab or Unani/Tibb (South Asia) (Ansari and Inamdar, 2010; Ansari, 2010).

Caesalpinia bonducella (CBC; Karanjwa) is an important medicinal plant extensively distributed throughout the coastal region of India, Burma, Sri Lanka, and in other tropical and subtropical regions of the world. It is an irregular thorny shrub with large bipinnate leaves. Its flowers are yellow and fruits are inflated pods having 1–2 seeds (Kapoor, 2008; Prajapati et al., 2006).

The plant is claimed to have multiple therapeutic properties like antidiuretic, anthelmintic and antibacterial, anti-anaphylactic and antiviral, antiasthmatic, antiamebic, and anti-estrogenic. Blood the sugar-lowering activity of *Caesalpinia bonducella* (CBC) has been primarily evaluated with significant results in rabbit and rat models (Dhar et al., 1968; Rao et al., 1994). In the present study, we examined the

analgesic and anti-inflammatory activities of aqua of CBC leaf.

Inflammation is a pathophysiological response of living tissue to injuries that leads to the local accumulation of plasmic fluid and blood cells and is typically characterized by redness, swelling, pain, and heat. The complex events and mediators involved in the inflammatory reaction may induce, maintain or aggravate many diseases. Though studies have been continuing on inflammatory diseases and the side effects of the currently available anti-inflammatory drugs pose a major problem during their clinical uses. Thus, the development of newer and more substantial anti-inflammatory drugs with lesser side effects is necessary (Su et al., 2012). Non-steroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, are prescribed globally for the management of pain, inflammation, and fever, as well as cardiovascular protection. But their uses were limited because of the key fact with gastrointestinal damage regardless of NSAIDs have provided effective management of pain and inflammation highly (Scheiman, 2001). In addition kidney damage, increase in blood pressure, and some other cardiovascular problems have been found with NSAIDs (Burke et al., 2006). Consequently, during the past decades, many researchers have focused on medicinal plants with fewer side effects for patients to develop anti-inflammatory and analgesic drugs.

The leaves of this plant are traditionally used for the treatment of tumors, inflammation, and liver disorders. It has also been recognized for multiple therapeutic properties that include antipyretic, antidiuretic, anthelmintic, antibacterial, anticonvulsant, anti anaphylactic, antidiarrheal, antiviral, antiasthmatic, anti-inflammatory, antiamoebic, antiestrogenic, nematocidal, antihyperglycemic, and abortifacient activities (Raghunathan and Mitra, 1982). In the present study, we examined the analgesic and anti-inflammatory activities of aqua of CBC.

MATERIALS AND METHODS

Collection and authentication of plant

CBC leaves were collected from Jamia Hamdard Botanical Garden, New Delhi, India. The authenticity and identity of the drugs were confirmed on the basis of the classical description in Unani literature at the Department of Ilmul Advia, Faculty of Medicine (Unani), Jamia Hamdard, New Delhi, and modern botanical information was established by the Department of Botany, Faculty of science Jamia Hamdard. A voucher specimen of the test drugs has been retained and deposited in the Department of Ilmul Advia, Faculty of Medicine (Unani), Jamia Hamdard, New Delhi.

Drugs and chemicals

Carrageenan and indomethacin were purchased from Sigma-Aldrich, St. Louis, MO, USA. Acetic acid was purchased from Pure Chem. Ltd., India.

Preparation of extract

Aqua of CBC leaves: The dried CBC leaves were distilled three times by distillation process with distilled water (8:2) for 8 hrs and the evaporation is collected in the form of aqua (arq).

Experimental animals

All the experiments were carried out in albino rats of Wistar strain (150-250 gm) of either sex, supplied by the Central Animal House facility of Jamia Hamdard, New Delhi. All animals were housed in groups of 4-6 in propylene cages and maintained on a standard pellet diet and tap water ad libitum. The animals were kept under standard laboratory conditions. The experiments were performed in accordance with the guidelines for the care and use of laboratory animals, laid down by the committee for the purpose of control and supervision of experiments on animals (CPCSEA), Ministry of Social Justice and Empowerment, Govt. of India, Jan. 2000. Ethical norms were strictly followed during all experimental procedures.

Analgesic activity

Acetic acid-induced writhing test

Analgesic activity was assessed by an abdominal writhing test using acetic acid (Turner, 1965). Albino rats of either sex weighing 150-250 g fasted overnight with *ad libitum* access to water. The animals were divided into six groups (n=6 each) viz.; group I- acetic acid control (normal saline, 10 ml/kg, p.o.), group II-indomethacin solution (20 mg/kg, p.o.), group III-CBC-I (7 ml/kg, p.o.), group IV-CBC-II (10.5 ml/kg, p.o.), group V-CBC-III (14 ml/kg, p.o.).

In the writhing test, 0.2 ml of 0.6 % acetic acid solution was injected intraperitoneally and the number of writhes was counted starting 5 min after injection for a period of 20 minutes. Indomethacin (20 mg/kg, p.o.), was used as a standard drug, and the test drug CBC in leaf aqua form was administered by the intragastric route 1 hour before acetic acid injection.

Hot plate test

Analgesic activity was further assessed by hot plate latency assay (Turner, 1965). Albino rats of either sex weighing 150-250 g fasted overnight with *ad libitum* access to water.

The rats were divided into six groups (n = 6 each) *viz.*;

Group I control (normal saline 10 ml/ kg, p.o.)
Group II indomethacin (20 mg/ kg, p.o.)
Group III CBC-I (7 ml/ kg, p.o.)
Group IV CBC-II (10.5 ml/ kg, p.o.)
Group V CBC-III (14 ml/ kg, p.o.)

In this system, rats in groups I and II were given doses of normal saline (10 ml/ kg,p.o.) and indomethacin (20 mg/ kg,p.o.) independently. The rats in Group III-V were given CBC in the form of splint aqua. Rats from each group were placed on the hot plate after the administration of the treatment medicine and the response time for the rats to lick the paw or jump from the hot plate was taken as the latency (s). This was also repeated at 60 and 90 minutes from the exact time given. The average latency was determined from the six rats in each group. The temperature of the hot plate was maintained at 55 ± 1º C. The cut-off time was kept at 20 seconds.

Anti-inflammatory study

Carrageenan- induced paw edema test

Inflammation was produced by administering0.1 ml of (1) carrageenan into thesub-plantar face of the rat hind paw (Winter et al., 1962). Albino rats of either gender weighing 150-250 g fasted overnight with ad libitum access to water.
The rats were divided into six groups (n = 6 each) *viz.*;

Group I carrageenan control (normal saline 10 ml/ kg,p.o.),
Group II indomethacin (20 mg/ kg, p.o.),
Group III CBC-I (7 ml/ kg, p.o.),
Group IV CBC-II (10.5 ml/ kg,p.o.),
Group V CBC-III (14 ml/ kg, p.o.),

In this trial, all drugs were given orally. One hour later all rats were injected with0.1 ml of 1 Carrageenan solution in the sub-plantar aponeurosis of the left hind paw and the paw volume was measured plethysmometrically at 1 hr, 3 hr, and 5 hr.
Indomethacin (20 mg/ kg, p.o.) was used as a standard drug and the test drug CBC in leaf aqua form was administered by the intragastric route 1 hr before carrageenan.

Safety of drugs on gastric mucosa

Assessment of the safety of drugs on the gastric mucosa of rats

This approach was performed to assess the safety of the test drugs on the gastric mucosa of rats. In this method albino rat of either gender weighing 150-250 g fasted overnight with ad libitum access to water.

The animals were divided into three groups (n = 6 each) viz.:
Group I: indomethacin (20 mg/ kg, p.o.)
Group II: CBC (14 ml/ kg, p.o.)

In this experiment, higher doses of drugs were given orally. After 5 hours animals were sacrificed by an overdose of ether vapors and the stomachs were removed, opened and the sum of the length of lesions was estimated for ulcer index given below.

Erosions	*Score*
1 mm or lower	1
1 mm to 2 mm	2
More than 2 mm	3

The overall score was divided by a factor of 10, which was designated as ulcer index (Main and Whittle, 1975).

The drug was administered orally, the veritably common route for administration of the drug in Tibb-e-Unani. The test drug extract was dissolved in distilled water immediately before the administration.

As the dose of CBC leaves is recommended as 5-7 g each in classical Unani literature for human beings, both the higher and lower doses were taken for reasoning the dose for animals in the present study.

The animal dose was calculated by multiplying these doses by applicable conversion factors (Ghosh, 1984). The leaf aqua of the test drugs was given in three different doses i.e. 7 ml/ kg,p.o.;10.5 ml/ kg,p.o. and 14 ml/ kg,p.o.

Statistical analysis

All the values are expressed as mean ± S.E.M. The statistical significance was determined by ANOVA followed by Dunnett's test. Values $p<0.05$ were considered as significant.

RESULTS

Analgesic study

Effect of aqua of CBC leaf on acetic acid- induced writhing test in rats

There was a significant reduction in the number of writhing in 20 minutes observed. The mean score for writhing was diminished by 23.45, 34.33, 42.21, and 54.69 in CBC and indomethacin treated groups respectively over the score of the control group. The diminished score for writhing is statistically significant at both doses as shown in Table 1.

Effect of CBC leaf aqua on hot plate test in rats

There was a significant increase in the reaction time observed for 30 min, 60 min, and 90 min. In comparison to the control group, aqua of the test drug (CBC) in the doses of 7 ml/ kg and10.50 ml/ kg and 14 ml/ kg showed a significant increase in the reaction time at 30min., 60min., and 90 min. The standard drug, indomethacin 20 mg/ kg showed a significant increase in the reaction time at 30 min, 60 min, and 90 min ($p<0.01$). The increased reaction time for hot plate is statistically significant at both doses as shown in Table 2.

Table 1: Effect of CBC leaf aqua on acetic acid-induced writhing test.

Group	Treatment	Dose	Number of writhes in 20 min	% variation
I	Acetic acid control	10 ml/kg	10.66 ± 0.33	--
II	Indomethacin	20 mg/kg	4.83 ± 0.16**	54.69%
III	CBC-I	7 mg/kg	8.16 ± 0.03*	23.45%
IV	CBC-II	10.5 mg/kg	7 ± 0.25**	34.33%
V	CBC-III	14 mg/kg	6.16 ± 0.30**	42.21%

CBC: *Caesalpinia bonducella*

Values are expressed as mean ± S.E.M. (n= 6),

**p < 0.01, compared with acetic acid control, ANOVA followed by Dunnett's test.

Table 2: Effect of *Caesalpinia bonducella* leaf aqua on hot plate test in rats.

Group	Treatment	Dose	Reaction time (s)		
			30 min	60 min	90 min
I	Control	10 ml/kg	3.83 ± 0.47	4.16 ± 0.47	3.83 ± 0.30
II	Indomethacin	20 mg/kg	9.33 ± 0.49**	9.33 ± 0.80**	10.16 ± 0.30**
			(143.6%)	(124.27%)	(165.27%)
III	CBC-I	7 mg/kg	3.33 ± 0.42*	6.33 ± 0.33	7.5 ± 0.42**
			(13.05%)	52.16%	(95.82%)
IV	CBC-II	10.5 mg/kg	4.5 ± 0.22*	8.16 ± 0.40*	7.80 ± 0.48**
			(17.49%)	(96.15%)	(103.65%)
V	CBC-III	14 mg/kg	5.5 ± 0.22**	9.06 ± 0.55*	10.13 ± 0.26**
			(43.60%)	(117.78%)	(164.49%)

CBC: *Caesalpinia bonducella*

Values are expressed as mean ± S.E.M. (n= 6),

*p < 0.05, **p < 0.01, compared with control, ANOVA followed by Dunnett's test.

Anti-inflammatory

Effect of CBC leaf aqua of carrageenan- induced hind paw edema in rats

A significant reduction in the paw volume was observed at Ist, 3rd, and 5th hr. In comparison to the control group, aqua of the test drug (CBC) in the doses of 7 ml/ kg and10.5 ml/ kg and 14 ml/ kg showed a significant reduction ($p<0.01$) in the paw volume at 1st, 3rd, and 5th hr. The standard drug, indomethacin 20 mg/ kg showed a significant drop in paw volume at 1st hr ($p<0.01$), 3rd hr ($p<0.01$) and 5th hr. ($p<0.01$) respectively.

The reduction in the paw volume is statistically significant at both middle and advanced boluses as shown in Table 3.

Table 3: Effect of aqua leaf of *Caesalpinia bonducella* on carrageenan-induced hind paw edema in rats.

Group	Treatment	Dose	Reaction time (s)			
			0 hr	1st hr	3rd hr	5th hr
I	Carrageenan control	10 ml/kg	0.8 ± 0.3	1.8 ± 0.03	1.86 ± 0.02	1.71 ± 0.04
II	Indomethacin	20 mg/kg	0.83 ± 0.04	1.43 ± 0.05**	1 ±0.04**	0.8 ± 0.03**
				(20.55%)	(46.23%)	(53.21%)
III	CBC-I	7 mg/kg	0.71 ± 0.04	1.65 ± 0.02**	1.75 ±0.02**	1.53 ±0.02**
				(8.33%)	(5.91%)	(10.52%)
IV	CBC-II	10.5 mg/kg	0.73 ± 0.04	1.56 ± 0.03**	1.53 ± 0.02*	1.3 ± 0.03**
				(13.33%)	(17.74%)	(23.97%)
V	CBC-III	14 mg/kg	0.71 ± 0.03	1.38 ± 0.05**	1.3 ± 0.02**	1.15 ±0.02**
				(23.33%)	(30.10%)	(32.74%)

CBC: *Caesalpinia bonducella*

Values are expressed as mean ± S.E.M. (n= 6),

*p < 0.05, **p < 0.01, compared with carrageenan control, ANOVA followed by Dunnett's test.

Assessment of the safety of test drugs on the gastric mucosa of rats

This method was employed to assess the safety of test drugs on the gastric mucosa of rats. In this approach, only the high dose of the test drugs was given. The drugs were given to the groups orally as under:

In this method, the indomethacin (20 mg/ kg) produced ulcers on the gastric mucosa but the test drugs (CBC) caused no ulcers at all as shown in Table 4.

Table 4: Assessment of the safety of test drugs on gastric mucosa of rats

Group	Dose (mg/kg)	Ulcer index
I	20	5.4
II	14 mg/kg	0

CBC: *Caesalpinia bonducella.*

DISCUSSION

The search for screening and development of drugs for anti-inflammatory activity is an unending problem. There is much hope of finding anti-inflammatory drugs from indigenous plants, as these are still used in therapeutics despite the progress made in conventional chemistry and pharmacology for producing effective drugs. Literature survey reveals that the species of 96 genera belonging to 56 families contain anti-inflammatory agents (Handa and Kaul, 1996).

The Unani herbal drug *Caesalpinia bonducella* (Karanjwa) is used individually for various anti-inflammatory disorders. *Caesalpinia bonducella* (CBC) has been used for centuries in the Unani system of medicine as Muhallil (Anti-inflammatory) and Musakkin (analgesic) (Ghani, 1921; Ibn-e-Sina, 1927).

The analgesic qualities were further investigated utilising sensitive models capable of producing various levels of painful stimuli (in thermal stimulus and chemically induced tissue damage). The analgesic activity of rats of both sexes was tested using an abdominal writhing test with acetic acid and a hot plate test (Turner, 1965).

Acetic acid-induced abdominal constriction is a sensitive technique for determining peripherally acting analgesics. The response is thought to involve local peritoneal receptors. A significant decrease in the number of writhings in 20 minutes was observed. The mean score for writhing was decreased by 23.45%, 34.33%, 42.21% & 54.69% in standard (indomethacin) lower middle and higher doses of an aqua form of CBC leaf respectively over the score of the control group. The decreased score for writhing was statistically significant at all the doses (p< 0.01).

In the hot plate test, nociceptive reaction towards thermal stimuli in rats is a well-validated model for detection of opiate analgesic as well as several types of analgesic drugs from spinal origin (Adzu et al., 2003). At 30 minutes, 60 minutes, and 90 minutes after the thermal stimulus, a substantial increase in reaction time was seen at various dose levels of aqua of CBC leaf (7, 10.50, and 14 mg/kg). The nociception inhibition of

thermal stimulus was exhibited at a lower dose of the extract is 95.82%, at & at higher dose 164.49% at 90 min which is comparable to indomethacin (165.27%). These findings suggest that the test drug exerts an analgesic effect similar to non-steroidal anti-inflammatory drugs. Thus the anti-nociceptive activity shown by CBC in aqua on a hot plate and acetic acid-induced writhing test might possess centrally and peripherally mediated anti-nociceptive properties.

Anti-inflammatory agents have widely been incriminated as one of the important causes of gastritis and gastric ulceration (peptic ulcers). The gastric lesions produced are the result of the prostaglandin inhibitory effect of anti-inflammatory agents, produced in the cyclo-oxygenase pathway of arachidonic acid metabolism. Prostaglandins generated through the cox-1 enzyme pathway have got a gastroprotective role and inhibition of cyclo-oxygenase results in the depletion of both the cox-1 and cox-2 enzymes, hence devoiding mucosal barrier from the protective effect of cox-1 mediated prostaglandins. In view of this, the drug was investigated for the gastric irritation potential also. The results of the study revealed that no gastric irritation sign was observed whereas the Indomethacin produced some ulcers.

The impact of the test medication extract was determined using carrageenan-induced paw edema. on acute inflammation. Carrageenan-induced paw inflammation is a test largely used to study both steroidal and non-steroidal anti-inflammatory drugs (Vinegar et al., 1987).

In the present study, the aqua of CBC leaf at various dose levels (7, 10.50, and 14 mg/kg) showed significant anti-inflammatory activity on carrageenan-induced edema in rats in a dose-dependent manner. CBC leaf at 7 mg/kg produced a significant inhibition ($p< 0.01$) of 8.33%, 5.91.48% and 10.52% at 1st hour, 3rd hour, and 5th hour respectively while at the dose of 10.50 mg/kg also produced significant inhibition ($p < 0.01$) of 13.33%, 17.74%, and 23.97% at 1st hour, 3rd hour, and 5th hour respectively and at higher dose it produced significant inhibition ($p < 0.01$) of 23.33%, 30.10% and 32.74% at 1st hour, 3rd hour and 5th hour respectively. The standard drug, indomethacin (20 mg/kg) showed an inhibition of 20.55% ($p< 0.01$), 46.23% ($p< 0.01$) and 53.21% ($p< 0.01$) at 1st hour, 3rd hour, and 5th hour respectively.

Drugs might be having different compounds responsible for the inhibition of different phases of carrageenan-induced inflammation. The higher degree of inhibition in the 5th hour shows that the drug might be interfering with prostaglandins i.e. the medication may be inhibiting prostaglandin-induced edoema in rats' rear paws. The inhibition at the 1st hour and 3rd hour may be due to interfering of the drug with histamines and serotonin-induced vascular changes, mobility of polymorphonuclear leucocytes, and the exudates that follows, both of which are signs of acute inflammation..

Thus, the test drug CBC leaf may be considered safer for use as compared to indomethacin, which although having well anti-inflammatory and analgesic activity produces gastric ulcers.

The ability of the aqua of leaf CBC to suppress abdominal writhes, increase pain threshold latency, inhibition of the phases of carrageenan-induced inflammation confirms the analgesic and anti-inflammatory properties. These findings justify the traditional use of this plant in the treatment of pain and other inflammatory conditions and validate its claim of being used for the said purpose in folklore medicine.

CONCLUSION

Based on the results of the present study, it can be concluded that the aqua of *Caesalpinia bonducella* leaf has potential activities in a dose-dependent manner against analgesic and anti-inflammatory activity. Hence, the present study gives a scientific approach to *Caesalpinia bonducella* leaf in consequent health benefits.

CONFLICT OF INTEREST

None Declared

REFERENCES

Ansari JA, Inamdar NN. The promise of traditional medicines. International Journal of Pharmacology. 2010;6:808-812.

Ansari JA. Therapeutic approaches in management of drug-induced hepatotoxicity. Journal of Biological Sciences. 2010;10:386-395.

Kapoor LD: Handbook of Ayurvedic Medicinal Plants. Boca Raton: CRC Press LLC. First Indian Reprint, Herbal Reference Library, Replika Press Pvt. Ltd., India, 2008, pp 88.

Prajapati ND, Purohit SS, Sharma AK, Kumar T: A Handbook Of Medicinal Plants A Complete Source Book. Agrobios, Jodhpur, India: Hindustan Printing Press, 2006, pp 100.

Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN, Roy C. Screening of Indian plants for biological activity. Indian Journal of Experimental Biology. 1968;6:232–247.

Raghunathan K, Mitra, R: Pharmacognosy of Indigenous Drugs. Central Council for Research in Ayurveda and Siddha, New Delhi, India. 1982, pp 484–510.

Rao VV, Dwivedi SK, Swarup D. Hypoglycemic effect of *Caesalpinia bonducella* in rabbits. Fitoterapia, 1994;65:245–247.

Su S, Hua Y, Wang Y, Gu W, Zhou W, Duan JA, et al. Evaluation of the anti-inflammatory and analgesic properties of individual and combined extracts from Commiphora myrrha, and Boswellia carterii. Journal of Ethnopharmacology. 2012;139:649-56,.

Scheiman JM. The impact of nonsteroidal anti-inflammatory drug-induced gastropathy. American Journal of Managed Care. 2001;7:S10–S14.

Burke A, Smyth E, Fitzgerald GA. Analgesic– antipyretic agents: pharmacotherapy of gout. In: Brunton, L.L., Lazo, J.S., Parker, K.L. (Eds.), Goodman and Gilmans the Pharmacological Basis of Therapeutics. McGraw Hill, New York, 2006, pp 706.

Turner RA: Analgesics: Screening Methods in Pharmacology. Academic Press, New York, 1965, pp 100.

Winter CA, Risley EA, Nuss GW. Carrageenan-induced oedema in hind paw of the rats as an assay for anti-inflammatory drugs. Proceeding of Social, Experimental and Biological Medicine. 1962;111:544–547.

Main IHM, Whittle BJR. Investigation of vasodilator and antisecretory role of prostaglandins in the rat gastric mucosa by use of non-steroidal anti-inflammatory drugs. British Journal of Pharmacology. 1975;53:217-224.

Handa SS, Kaul MK: Supplement to cultivation and Utilization of plants. Jammu, India: RRL, Jammu Tawi 1996.

Ghani MN: Khazain-ul-Advia (Vol. 3). Lahore, Pakistan: Shaikh Mohammad Bashir & Sons. 1921.

Ibn-e-Sina: Alqanoon fit Tibb (Vol. II). (G H Kantoori, Trans.) Lahore: Shaikh Mohammad Bashir & Sons, 1927.

Adzu B, Amos S, Kapu SD, Gamaniel KS. Anti-inflammatory and anti-nociceptive effects of Sphaeranthus senegalensis. Journal of Ethnopharmacology. 2003; 84:169–173.

Vinegar R, Truax JF, Selph JL, Johnston PR, Venable AL, McKenzie KK. Pathway to carrageenan-induced inflammation in the hind limb of the rat. Federation Proceedings. 1987;46:118–126.

Ghosh MN. Fundamentals of experimental pharmacology. 2nd ed. Calcutta, India: Scientific Book Agency; 1984.