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Research Article

ANALGESIC AND ANTHELMINTIC ACTIVITY OF VARIOUS EXTRACTS OF ANDROGRAPHIS PANACULATA NEES. STEM

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ABSTRACT

Objective: The aim of the present study was to evaluate the analgesic and anthelmintic activity of various extracts of *Andrographispanaculata*Nees. stem.

Methods: The bark of Andrographis*panaculata*Nees.was extracted with 95% ethanoland ether at 55°C and evaluate for their analgesic activity in mice using the tail-flick and acetic acid-induced writhing method and anthelmintic activity.

Results: Ether extract exhibits potent analgesic activity in tail-flick test at 200mg/kg two hours after administration in compare with 95% ethanolic extract, whereas 95% ethanolic extract exhibits significant analgesic activity in acetic acid-induced writhing test at 100 mg/kg.For anthelmintic activity,test results revealed that 95% ethanolic extract of *Andrographispaniculata*(N) not only demonstrated paralysis, but also caused death of worms especially at higher concentration of 1% g/dl in shorter time as compared to reference drug Albendazole.

Conclusion: Phytochemical analysis illustrated that the extract contained compounds such as alkaloids, tannins, flavonoids and steroids. It is conceivable therefore that the extracts of *Andrographispaniculata*(N) contain certain biologically active compounds that might be responsible for the both analgesic and anthelmintic activity.

Keywords: *Andrographis paniculata*, Diclofenac sodium, Albendazole, Anthelmintic, Analgesic.

INTRODUCTION

Traditional medicine worldwide is being re-evaluated by extensive research on different plant species and their therapeutic principles. Over the past twenty years, interest in medicinal plants has grown enormously from the use of herbal products as natural cosmetics and for self-medication by the general public to the scientific investigations of plants for their biological effects in human beings. Beyond this pharmaceutical approach to plants, there is a wide tendency to utilize herbal products to supplement the diet, mainly with the intention of improving the quality of life and preventing the diseases of elderly people[1]. India has been identified as a major resourceful area in the traditional and alternative medicines globally.

*Andrographispaniculata*Nees.is an herbaceous plant in the family Acanthaceae, native to India and Sri Lanka. It is widely cultivated in Southern and South-eastern Asia, where it is used to treat infections and some diseases, often being used before antibiotics were created. Diterpenoids andflavanoids are the main chemical constituents of *Andrographispaniculata*and these compounds are believed to beresponsible for the biological activities of the plant. It is widely used in Chinese and Ayurvedic medicine for thetreatment of gastric disorders, infectious diseases andcommon colds. It has multiple pharmacological properties such as immunostimulant [2] and used for myocardial ischemic [3], pharyngotonsillitis [4], respiratory tract infections [5] and common cold [6]. It possesses antimicrobial, anti-inflammatory [7], hypotensive [8], antihyperglycemic [9, 10]; oxygen radical scavenging, atherosclerotic [11], anti-malarial activity [12], anti-HIV [13], anti-platelet aggregation [14], hepatic lipid peroxidation protective [15], hepatoprotective [16], choleretic effect [17]and anticancer effects [18-21]. The ability of *Andrographispaniculata*to lower fever has been demonstrated independently in several reports. There is very limited data available on its analgesic and anthelmintic activity. In this paper, we would like to describe the extraction and evaluation of analgesic and anthelmintic activity of bark extract of *Andrographispaniculata*(N).

MATERIAL AND METHOD

Drug and plant material

Reference standard Diclofenac sodium and Albendazolewas procured from Cipla Pharmaceuticals, Mumbai, as a gift sample.The bark of *Andrographispaniculata*(N) was collected from Tawang forest Divisions of Arunachal Pradesh in the month of September. The plant was identified and authenticated by the Botanist of Shibpur Botanical Garden, Kolkata (voucher specimen no. SBG/11-0785).

Preparation of extract

Fresh bark was cleaned, dried under shade at temperature 40±2°C and powdered by a mechanical grinder and stored in an air tight container till further successive extraction. The dried and powdered bark of *Andrographispaniculata*(N) was subjected to Soxhlet extraction with 95% ethanol andether at 55°Cfor 6 hr. Then the extract was concentrated by using rotary vacuum evaporator at low temperature. They were then weighed and percentage of different extractive values was calculated with respect to air-dried substance. The extract was purified by preparative TLC using n-butanol and glacialacetic acid as mobile phase.

Preliminary phytochemical screening

All the extracts were subjected to preliminary phytochemical qualitative screening for the presence or absence of various primary or secondary metabolites following standard procedures [22, 23].

Experimental animals

Adult Swiss albino mice of either sex weighing 25 to 30 g maintained in our college animal house were used for the study. The selected animals were maintained by giving pelleted diet, water *adlibitum* and kept in 12 hr/12 hr light/dark cycle. The animals were divided into six groups each containing six mice. All the animal experiments were performed following the approval of study protocols by the Institutional Animal Ethics Committee (HPI/12/60/IAEC, 012).

Acute toxicity study

The study was carried out according to Organization of Economic Co-operation and Development (OECD) guidelines 423 [24]. Nine female Swiss albino mice weighing 25-30 g were taken andextracts were administered orally to animals at a doseof 2000 mg/kg in 0.3% w/v carboxy methyl cellulose sodium. Then the animals were observedfor mortality and morbidity at 0, 0.5, 1, 2, 4, 6, 8, 12and 24

hr. Food was given to the animals after 4 hr ofdosing and the body weight was checked at 6 hr afterdosing. Morbidity like convulsions, tremors, grip strength, lethargy, ptosis and pupil dilation wereobserved. The animals were observed twice daily for 14 days and body weight was noted.

Analgesic activity

Analgesic activity was assessed by Tail-flick method[25]andAcetic acid-induced writhing method [26].

Tail-flick method

Swiss albino mice (25-30 g) of either sex (reaction time: 3-4 sec) were divided into groups of 6 each. Diclofenac sodium (50 mg/kg, p.o.) was used as standard. The tail-flick latency was assessed by the analgesiometer (Techno, India). The magnitude of the current which was passing through the naked nichrome wire was kept constant at 6 ampere. The tail skin was kept at a distance of 1.5 cm from the heat source. The radiant heat (55±2 °C) in the tail was applied and maintained at 2.5 cm measured from the root of the tail. In order to avoid the tissue damage, the cut of reaction time was kept at 10-13 sec. The mean scores in control, standard (Diclofenac sodium), and test groups were recorded and tabulated in Table 1.

Acetic-acid induced writhing method

In the writhing test adult Swiss albino mice(25-30 g) of either sex were used in six groups of 6each. Diclofenac sodium (50 mg/kg, p.o.) was usedas standard. 1% w/v gum acacia was used as controland 95% ethanolic and etherextract (100 and 200 mg/kg,p.o.) was used as treatment for other four groups.Then 1% v/v aqueous acetic acid was administeredintraperitonially to all the groups to produce writhe.Test substances were administered 30 minutes beforeinjection of acetic acid. Animals were keptindividually under glass jar for observationimmediately after acetic acid injection for 20 minute period. Onset on writhes was noted and the number of abnormal constrictions, trunk twist response and extension of hind limbs were recorded. The meanwrithing scores in control, standard (Diclofenacsodium), and test groups and the percentage of writhing were calculated and tabulated in Table 2.

Anthelmintic activity

The extracts of *Andrographispaniculata*(N)were tested for anthelmintic activity according to method described in detail by Kuppast and Nayak[27]. *Pheretimaposthuma* (earthworms obtained from Shibpur Botanical Garden, Kolkata) of nearly equal size (6±1 cm) were selected randomly for present study.

The worms were acclimatized to the laboratory condition before experimentation. The earthworms were divided into six groups of six earthworms in each. Albendazole diluted with normal saline solution to obtained 0.1, 0.2, 0.5 and 1% w/v served as standard and poured into petridishes. The extracts were prepared in minimal quantity of ethanol and diluted to prepare four concentrations *i.e.*,0.1, 0.2, 0.5 and 1% w/v for each extract. Normal saline serves as control. Six earthworms at room temperature. The time taken for complete were nearly equal size (6±1 cm) are taken for each concentration and placed in petridishes paralysis and death are recorded. The mean paralysis time and mean lethal time for each sample was calculated(eachreading were taken triplicate). The time taken for worms to become motionless was noted as paralysis time and to ascertain death, each worm was frequently applied with external stimuli which stimulates and induce movement in the earthworms, if alive. The results were recorded and tabulated in Table 3.

Statistical analysis

Values are expressed as mean±SEM and data was analysed by ANOVA followed by Dunnet's test. $p<0.01$ was considered as significant.

Table 1: Analgesic effect of *Andrographis paniculata* (N) extracts on thermally induced nociception in mice

S. No.	Group	Dose/kg body wt.	Reaction time in sec (Mean±SEM)		
			Tail flick at 0.5h(sec)	Tail flick at 1.0h(sec)	Tail flick at 2.0h(sec)
1	Control	20 ml	3.28±0.01	3.60±0.03	3.70±0.02
2	Diclofenac sodium	50mg	9.07±0.02*	10.55±0.02*	11.22±0.02*
3	95% Ethanolic extract (A1)	100mg	9.02±0.01*	10.02±0.01*	11.98±0.02*
4	95% Ethanolic extract (A2)	200mg	7.98±0.03*	8.25±0.09*	9.34±0.09*
5	Ether extract (A3)	100mg	7.63±0.008*	8.25±0.06*	8.36±0.37*
6	Ether extract (A4)	200mg	9.01±0.008*	10.83±0.008*	12.62±0.07*

n=6 in each group. * p< 0.01 compared to control

Table 2: Analgesic effect of *Andrographispaniculata* (N) extracts on acetic acid-induced writhing in mice

S. No.	Group	Dose/kg body wt.	Number of writhing (Mean ± SEM)	% inhibition of writhing
1	Control	20 ml	73.33±2.37	------
2	Diclofenac sodium	50mg	24.17±1.78*	67.04
3	95% Ethanolic extract (A1)	100 mg	36.50 ± 4.26*	50.23
4	95% Ethanolic extract (A2)	200 mg	55.33 ± 3.89*	24.55
5	Ether extract (A3)	100 mg	40.67 ± 1.89*	44.54
6	Ether extract (A4)	200 mg	38.50 ± 1.38*	47.49

n=6 in each group. * p< 0.01 compared to control

Table 3: Anthelmintic activity of Analgesic effect of *Andrographis paniculata* (N) extracts

Group	Time for paralysis (min)[a]				Time for death (min)[a]			
	Concentration (g / dl)				Concentration (g / dl)			
	0.1	0.2	0.5	1.0	0.1	0.2	0.5	1.0

95% Ethanolic extract	3.25 ± 0.17	2.24 ± 0.12	1.27 ± 0.16	1.22 ± 0.16	7.13 ± 0.26	5.09 ± 0.21	3.15 ± 0.23	2.28 ± 0.15
Ether extract	2.39 ± 0.06	2.08 ± 0.18	1.51 ± 0.03	1.18 ± 0.10	6.15 ± 0.27	4.32 ± 0.09	3.25 ± 0.10	2.45 ± 0.08
Negative control (Dimethyl sulphoxide)	24.47 ± 0.05	22.09 ± 0.11	20.13 ± 0.02	17.19 ± 0.21	38.09 ± 0.09	37.12 ± 0.22	34.23 ± 0.17	30.09 ± 0.11
Albendazole	2.06 ± 0.03	1.51 ± 0.19	1.25 ± 0.007	0.58 ± 0.04	6.02 ± 0.21	4.42 ± 0.16	4.04 ± 0.03	2.47 ± 0.03

[a]Mean ± SEM, n = 6in each group.

RESULT AND DISCUSSION

Preliminary phytochemical analysis showed the presence of alkaloids, flavonoids, steroids and tannins like phytoconstituents in the extracts of *Andrographispaniculata* (N). Some of these phytoconstituents may be responsible to show a potent analgesic and anthelmintic activity. The results of the present study confirm the analgesic activity of 95% ethanolic and ether extract of *Andrographispaniculata*(N) bark. The tail-flick and acetic acid-induced abdominal constriction method is widely used for the evaluation of peripheral antinociceptive activity [28] because it is very sensitive and able to detect antinociceptive effects of compounds at dose levels [29]. Local peritoneal receptors are postulated to be partly involved in the abdominal constriction response [30]. The method has also been associated with direct stimulation of nociceptive afferent fibers due to pH reduction [31] and generation of prostanoids in general, for example, increased levels of PGE2 and PGF2a in peritoneal fluids [32] as well as lipoxygenase products [33]. NSAIDs inhibit cyclooxygenase enzyme in the peripheral tissues and therefore interfere with the mechanism of transduction of primary afferent nociceptors [34].

Mechanism of action of *Andrographispaniculata*(N) could be due to inhibition of synthesis of endogenous substance that excites pain nerve endings similar to NSAIDs. Previous studies have shown that it reduces PGE synthesis from macrophages[35] and its oral administration to mice suppresses acetic acid induced vascular permeability [36].The reduction in the number of writhing indicates *Andrographispaniculata*(N) might exert antinociceptive activity by inhibition of prostaglandin synthesis or by interfering direct stimulation of nociceptiveafferents in the periphery. The results also indicate that the peripheral analgesic activity of the *Andrographispaniculata*(N) at doses 100 and 200mg/kg was significance as compare to standard drug Diclofenac sodium at 50mg/kg (Table 1 and 2). Nevertheless, the reduction in writhing was comparable to standard drug. However, long term studies and studies on both pharmacokinetics and pharmacodynamics are required to conclude the above presumption.

Andrographispaniculata(N) was found to show a potent anthelmintic activity when compared to the standard drug. 95% Ethanolic extract of *Andrographispaniculata* at 1% g/dl concentration shows paralysis at 1.22 min and death 2.28 min, whereas etherextracts shows paralysis at 1.18 min and death 2.45 min respectively against the earth worm *Pheretimaprosthuma*. The reference drug Albendazole exhibited the same at 0.58 min and 2.47 min respectively (Table3). Albendazole exhibits anthelmintic activity by blocking glucose uptake and depletion of glycogen stores in test parasite. 95% Ethanolicextract of *Andrographispaniculata* not only demonstrated paralysis, but also caused death of worms especially at higher concentration of 1% g/dl in shorter time as compared to reference drug Albendazole. Phytochemical screening of the extracts revealed the presence of alkaloids, flavonoids, tannins and steroids. Tannins were shown to produce anthelmintic activities [37], chemically tannins are polyphenolic compounds [38]. It is possible that tannins contained in the extracts of *Andrographispaniculata*(N) produce similar effects. Reported anthelmintic effect of tannins, can bind to free proteins in the gastrointestinal tract of host animal [39] or glycoprotein on the cuticle of the parasite and may cause death. Further studies are under process to identify the possible phytoconstituents responsible for anthelmintic activity.

CONCLUSION

The traditional use of the whole plant of *Andrographispaniculata*(N) as analgesic and anthelmintic has been confirmed using the 95% ethanolic and ether extracts and showed good analgesic and anthelmintic activity. Further it would be interesting to isolate the responsible phytoconstituents which are responsible for both analgesic and anthelmintic activity and the mechanism of action, which is being attempted in the laboratory.

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