Research Article

Exploration of Analgesic, Antiinflammatory, Laxative, and Anthelmintic Activities of *Hygrophila phlomoides*

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ABSTRACT

To identify novel bioactivities, we studied analgesic, antiinflammatory, laxative, and anthelmintic properties of *Hygrophila phlomoides* (*H. phlomoides*) crude extract. The phytochemical study of *H. phlomoides* extract reflected the existence of numerous secondary metabolites such as reducing sugars, phenolic compounds, flavonoids, tannins, proteins, alkaloids, glycosides, saponins, steroids, terpenoids, and acidic compounds, which might be playing a role for its medicinal properties. The extract of *H. phlomoides* at 250 and 500 mg/kg exhibited significant writhing inhibition by 35.82% and 58.96%, respectively. *H. phlomoides* extract reflected significant antiinflammatory activity at 250 and 500 mg/kg in formaldehyde-induced paw edema up to 4 h. The experimental data exhibited that *H. phlomoides* extract at 250 and 500 mg/kg significantly increased stool production by 61.58% and 77.03%, respectively. In the anthelmintic study, *H. phlomoides* extract paralysed and killed the parasites dose-dependently. The outcome of this study indicated that the ethanol extract of *H. phlomoides* aerial parts possesses analgesic, antiinflammatory, laxative, and anthelmintic properties.

Keywords: *Hygrophila phlomoides*, Acanthaceae, analgesic, antiinflammatory, laxative, anthelmintic.

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INTRODUCTION

Nature has blessed us with a plethora of medicinal plants. The use of medicinal plants to treat diseases is as old as human civilization. The majority of medications are still derived from plants. People in third-world countries frequently rely on medicinal plants for disease cures due to the high cost of treatment. In developing countries, up to 80% of the population still uses herbal medicines for primary health care[1]. *Hygrophila phlomoides* (*H. phlomoides*) belonging to the family Acanthaceae, is about 1 m tall and, erect. Leaf-blade is elliptic, obovate, or oblong and flowers axillary, several clustered or in whorls upward. The plant is habitat in Cambodia, India, Bangladesh, Indonesia, Laos, Myanmar, Pakistan, Philippines, Thailand, and Vietnam[2, 3]. To date, no chemical compound or biological activities have been reported from the species. However, the genus has been identified with the presence of alkaloids, steroids, tannins, proteins, flavonoids, carbohydrates, fats, oils, glycosides, and phenolic compounds[4]. The genus was also found with analgesic, antiinflammatory, laxative, and anthelmintic potentialities[5, 6]. *Strobilanthes anamallaica* belongs to the same family and has been reported with laxative property[7]. Based on the literature review, *H. phlomoides* was selected to study the analgesic, antiinflammatory, laxative, and anthelmintic activities.

The pain had been regarded as a distressing sensory and emotional experience connected to real or potential tissue injury. An analgesic is a substance that, either centrally or peripherally, acts on the sensory nervous system to lessen or remove pain without appreciably affecting awareness. Non-steroidal antiinflammatory drugs (NSAIDs), opioids, and corticosteroids, which are frequently used in contemporary medicine to decrease pain and inflammation, only offer symptomatic relief. Additionally, using these medicines is linked to major side effects[8].

The local reaction of living mammalian tissues to harm caused by any substance is known as inflammation. The complex array of enzyme activation, mediator release, fluid extravasations, cell migration, tissue disintegration, and repair that the inflammatory response entails is usually triggered in the majority of disease conditions and is directed at the host's defense[9]. Synthetic medications, such as NSAIDs, opioids, and corticosteroids, are clinically the most significant medications used to treat inflammatory disorders. However, prolonged use of these medications may result in toxic side effects, such as gastrointestinal ulcers, bleeding, renal disorders, and other issues[10]. Even though synthetic medications currently rule the market, the possibility of some degree of harm still exists. Moreover, their prolonged use may cause severe adverse effects[11].

Laxatives, purgatives, and aperients are medicines that promote frequent bowel movements and soften faeces. Constipation is treated and/or prevented with them. Enemas may occasionally be used in addition to certain

stimulants, lubricants, and saline laxatives to help the colon empty for rectal and bowel examinations. Diarrhea may result from taking laxatives in sufficiently high doses[12]. Currently, lifestyle changes and dietary fiber consumption are utilized as traditional mainstays to manage constipation together with medicine. However, none of these choices result in satisfying answers[13-15].

Human helminth infections are among the most common infections that affect a huge portion of the global population. Even though the majority of helminth infections are often only found in tropical areas, they pose a serious health risk and increase the risk of malnutrition, anemia, eosinophilia, and pneumonia[16]. The population in endemic areas is most affected by the brutal morbidity caused by parasitic diseases[17]. The treatment of helminth disorders faces a major challenge because the gastro-intestinal helminths become resistant to the anthelmintic medications that are currently on the market[18].

Therefore, we sought to explore phytochemical analysis and look into the plant's analgesic, antiinflammatory, laxative, and anthelmintic properties based on literature reviews of the plant and the need for new treatments.

MATERIALS AND METHODS

Plant Collection, and Crude Extract Preparation

The aerial part of *H. phlomoides* was collected from the Khulna University campus. The collection took place in January 2018 at daytime. Any form of adulteration was strictly forbidden during collection. Experts at the Bangladesh National Herbarium in Mirpur, Dhaka, recognized the plant, and a voucher specimen (45951 DACB) was provided there for future use.

The desired aerial parts were freed of the undesirable elements, plants, and plant fragments. The plant underwent shade drying to prevent the breakdown of the active components. The dried aerial part was ground into a coarse powder and it was stored in an airtight container in a cool, dark, and dry environment. *H. phlomoides* powder weighing 100 g was placed in clean, glass container with flat bottom and allowed to soak in 600 ml of ethanol. The containers and its contents were sealed and kept for 15 days while being occasionally shaken and stirred. After that, a piece of clean cloth was used to perform a coarse filtration on the entire mixture. The filtrate was obtained and evaporated after it had been filtered via filter paper. It produced a paste concentrate that was greenish-black in color (crude extract yield 10.12%).

Phytochemical Tests

Identification of the types of chemicals present in the crude extract is crucial to assess the extract's pharmacological activity. Standard techniques were used to identify the chemical components of plant extract[19-21].

Animals

The experiment was conducted using young Swiss-albino mice (both male and female), aged 4-5 weeks, with an average weight of 28–35 g. The mice were purchased and collected from the International Centre for Diarrheal Disease and Research, Bangladesh (ICDDR,B). After being purchased, they were adapted for a week in a standard condition in the animal home of the pharmacy department at Khulna University in Bangladesh. The animals were kept at a normal day-night cycle and fed regular laboratory food and water. All of the tests were carried out in a quiet, secluded environment. Live parasites (nematodes) were procured from recently butchered calves at nearby abattoirs to conduct the anthelmintic test. Parasites were cleaned, then stored in 0.9 % phosphate-buffered saline (PBS), which was made with 8.01 g of sodium chloride, 0.20 g of potassium chloride, and 1.78 g of sodium biphosphate, and 0.27 g of potassium biphosphate in 1 litre of distilled water at 37±1 °C.

Analgesic activity

Test samples (*H. phlomoides* extract) at 250 and 500 mg/kg, a positive control (diclofenac sodium), and negative control (1% tween-80 in water) were administered orally. For the prescribed substances to be properly absorbed, a 30 minutes break was allowed. Then, acetic acid solution (0.7%) was injected intraperitoneally into each rat in a group. After a 5 minutes break for acetic acid absorption, the number of writhing was recorded for 15 minutes[22].

Antiinflammatory activity

The antiinflammatory potentiality of *H. phlomoides* extract was investigated utilizing the formaldehyde-induced paw edema in mice by Jahan et al., 2021[23]. Briefly, the test groups of mice received the extract at 250 and 500 mg/kg orally. Ibuprofen (100 mg/kg) and 1% v/v tween 80 (10 ml/kg) were given to mice in the positive control and negative control group, respectively. The right hind paw's linear circumference was then determined using a slide caliper. After 30 minutes, 0.1 ml of formalin (2% v/v) was administered into the mice's right hind paw's sub-plantar region to cause edema. The treated paw's linear circumference was recorded at the 1st, 2nd, 3rd, and 4th hours after formalin injection. Then, paw size change was estimated as = (paw size after formalin injection -paw size prior to formalin injection).

$$\% \text{ inflammation of paw edema} = \frac{inflammation\ of\ the\ test\ group}{inflammation\ of\ the\ control\ group} \text{ X } 100$$

% inhibition of inflammation = 100 - % inflammation

Laxative activity

This activity was investigated following the approach mentioned by Capasso *et al*. 1986 with minor modification[24]. The experimental mice were distributed into four groups comprising 6 in each group. The first group (control) was administered normal saline and the second group (standard) was administered bisacodyl. The other two groups were administered the plant extract in two different doses. The concentration of bisacodyl, as well as

the test extract, was determined in such a way that each mouse received 2 ml of solution consistently. Following 16 hours, the feces were weighed for each group and compared the test groups with the control and standard group[25].

Anthelmintic activity

Anthelmintic potentiality of the crude extract was assessed using live cattle parasites based on Utpal et al. 2020 with minor modification[26]. The parasites were separated into four test groups having six in each group. The standard albendazole at 15 mg/ml of 10 ml in PBS and extract at 25 and 50 mg/ml were prepared and put into petri dishes. Treatment for the control group included 0.1% tween-80 in PBS. The period of paralysis was noted, when no movement was visible unless violent shaking. The death time was measured when there was no movement in response to external stimulation, violent shaking, or immersion in warm water (50 °C). The anthelmintic effect was measured as the time needed to be paralyzed and death of parasites compared to control.

RESULTS

Profiling of phytochemicals

Preliminary phytochemical investigation of *H. phlomoides* extract revealed the existence of reducing sugars, phenolic compounds, flavonoids, tannins, proteins, alkaloids, glycosides, saponins, steroids, terpenoids, and acidic compounds.

Analgesic activity

The outcome of this study reflected that *H. phlomoides* ethanol extract at 250 and 500 mg/kg exhibited significant writhing inhibition by 35.82% and 58.96%, respectively while the writhing inhibition by standard, diclofenac sodium was found to be 79.10% at 25 mg/kg compared to the negative control**.** Therefore, it can be summarised that this extract shows dose-dependent analgesic activity.

Table 1: Effects of *H. phlomoides* extract on acetic acid-induced writhing of mice

Mice group with dose	% Writhing	% Writhing inhibition
Negative control, 1% tween-80 in water (10 ml/kg)	100	-
Positive control, diclofenac sodium Na (25 mg/kg)	20.9	79.10±0.75***
H. phlomoides extract (250 mg/kg)	64.18	35.82±0.58**
H. phlomoides extract (500 mg/kg)	40.04	58.96±0.71***

Values are expressed as mean ± standard error of the mean (n = 3); * indicates $p<0.05$, ** indicates $p<0.01$, and *** indicates $p<0.001$ when compared with control.

Antiinflammatory activity

Extract *H. phlomoides* showed significant antiinflammatory activity at 250 and 500 mg/kg in formaldehyde-induced paw oedema at 1 h, which persisted up to 4 h. Ibuprofen also showed a similar level of antiinflammation from 1 h onwards, which persisted up to 4 h after administration of 100 mg/kg per oral (Table 2).

Table 2: Antiinflammatory effect of *H. phlomoides* extract on formaldehyde-induced paw edema in mice

Mice group with dose	Time (hours)	Average paw volume	% Inhibition of inflammation
Negative control, distilled water (10 ml/kg)	1st	3.12	-
	2nd	2.56	-
	3rd	2.16	-
	4th	1.68	-
Positive control, Ibuprofen (100 mg/kg)	1st	1.96	37.18±0.160*
	2nd	1.36	46.87±0.066**
	3rd	0.96	55.56±0.117***
	4th	0.6	64.28±0.063***
H. phlomoides extract (250 mg/kg)	1st	2.3	26.28±0.089
	2nd	1.78	30.47±0.040
	3rd	1.46	32.41±0.060
	4th	1.1	34.52±0.063
H. phlomoides extract (500 mg/kg)	1st	2.06	33.97±0.075
	2nd	1.56	39.06±0.098
	3rd	1.2	44.45±0.089
	4th	0.8	52.38±0.089

Values are expressed as mean ± standard error of the mean; (n = 3); * indicates $p<0.05$, ** indicates $p<0.01$, and *** indicates $p<0.001$ when compared with control.

Laxative activity

The experimental data showed that *H. phlomoides* extract at 250 and 500 mg/kg exhibited a significant increase in stool production at 61.58% and 77.03%, respectively whereas the standard drug bisacodyl (10 mg/kg) caused an 80.7% increase in the stool production. Here, the total amount of produced stool was significant with soft consistency in comparison with the standard and negative control group (Table 3).

Anthelmintic activity

The parasites were both paralyzed and killed by the crude extract of *H. phlomoides*. These periods were noted and revealed to be dose-dependent. Paralysis times for parasites at 25 and 50 mg/ml of *H. phlomoides* extract were 24.55 and 16.47 minutes, respectively, while paralysis time for albendazole was 8.43 minutes. The death time for parasites at 25 and 50 mg/ml were 40.02

and 27.69 minutes, respectively, however, the time for albendazole was 15.21 minutes (Table 4).

Table 3: Laxative effect of *H. phlomoides* extract in experimental mice

Mice group with dose	Average weight of feces	% of increase in weight of feces
Negative control, Normal Saline (10 ml/kg)	0.58 ± 0.03	-
Positive control, bisacodyl (10 mg/kg)	3.01 ± 0.04	80.70 ± 1.17***
H. phlomoides extract (250 mg/kg)	1.5 ± 0.085	61.58 ± 0.283***
H. phlomoides extract (500 mg/kg)	2.5 ± 0.106	77.03 ± 0.156***

Values are expressed as mean ± standard error of the mean; (n = 3); * indicates $p<0.05$, ** indicates $p<0.01$, and *** indicates $p<0.001$ when compared with control.

Table 4: Anthelmintic effect of *H. phlomoides* extract

Mice group with dose	Mean time of paralysis (minutes)	Mean time of death (minutes)
Negative Control 0.1 % Tween-80 in PBS	-	-
Positive Control, albendazole (15 mg/ml)	8.43 ± 0.408*	15.21 ± 0.669***
H. phlomoides extract (25 mg/ml)	24.55 ± 0.488*	40.02 ± 0.841**
H. phlomoides extract (50 mg/ml)	16.47 ± 0.483**	27.69 ± 1.229***

Values are expressed as mean ± standard error of the mean; (n = 3); * indicates $p<0.05$, ** indicates $p<0.01$, and *** indicates $p<0.001$ when compared with control.

DISCUSSION

The preliminary phytochemical study of *H. phlomoides* crude extract revealed the existence of reducing sugars, phenolic compounds, flavonoids, tannins, proteins, alkaloids, glycosides, saponins, steroids, terpenoids, and acidic compounds. Among these phytochemicals, phenolic compounds, flavonoids, tannins, and alkaloids are the most beneficial for therapeutic activity. It has already been reported that polyphenolic compounds, such as phenolic acids, flavonoids, and tannins, exert multiple biological responses, including antioxidant, antiinflammatory, laxative, and anthelmintic activity[26]. Phytochemicals like terpenoids, flavonoids, and tannins contribute to analgesic activity[27, 28]. Therefore, the presence of different phytochemical groups in *H. phlomoides* extract assisted us to carry out various pharmacological activities

In the acetic acid-induced analgesic activity evaluation, acetic acid was injected into mice to cause pain of peripheral origin[29]. To discover promising peripherally acting antinociceptive compounds, this model is extremely useful for dosage where the analgesic and antiinflammatory properties of medicines would be unproductive in other pain models[30]. When acetic acid is injected intraperitoneally, peripheral nociception is activated through the direct stimulation of non-selective cationic channels or the indirect release of various endogenous mediators, including prostaglandins, cytokines, and bradykinin, along with higher production of the enzymes lipoxygenase (LOX) and cyclooxygenase (COX)[31], which stimulates nociceptive neurons sensitive to nonsteroidal antiinflammatory drugs[32]. Therefore, this study can be used to investigate novel NSAIDs. The analgesic potential of *H. phlomoides* extract was compared to that of diclofenac sodium in this experiment, which suggests that the extract may have peripheral anti-nociceptive properties. Its mode of action may involve a peripheral inhibition of LOX and/or COX, a decrease in prostaglandin synthesis, and intervention with the transduction phenomenon in primary afferent nociceptors. Phytoconstituents such as terpenoids, flavonoids, and tannins present in the extract of *H. phlomoides* could be responsible for analgesic activity.

The antiinflammatory study showed that *H. phlomoides* ethanol extracts have antiinflammatory characteristics. Alkaloids, flavonoids, tannins, steroids, and phenols are some of the polyphenolic chemicals that may be responsible for these activities[33]. Ibuprofen works by inhibiting COX enzymes, which transform arachidonic acid into prostaglandin H_2 (PGH_2). PGH_2 is then transformed by other enzymes into several different prostaglandins (mediators of pain, inflammation, and fever) and thromboxane A2. Ibuprofen is a nonselective COX inhibitor, similar to aspirin and indomethacin, as it inhibits both COX-1 and COX-2 cyclooxygenase isoforms[34]. The extract of *H. phlomoides* may show antiinflammatory activity following this mechanism.

Bisacodyl is a member of the polyphenolic group of stimulant laxatives. To cause a bowel movement, it works directly on the colon. It is frequently recommended for the treatment of constipation, the control of neurogenic bowel dysfunction, and as a bowel preparation measure before pathological tests such as colonoscopy[35]. The function of bisacodyl on the small intestine is minor; stimulant laxatives mainly stimulate evacuation of the colon[36]. In this study, *H. phlomoides* extract showed a significant increase in stool production in mice. *H. phlomoides* extract may act to follow the mechanism of bisacodyl, which could be due to the presence of polyphenolic compounds observed in our phytochemical study.

Nematodes called helminths are exceedingly prevalent and inhabit the gastrointestinal tracts of mammals. These parasites deprive their hosts' bodies of blood, nutrition, vitamins, and other essential elements, leading to the

development of various diseases. These protozoal diseases afflict around 3.5 million individuals[37]. Anthelmintic effects of plants are typically attributed to secondary metabolites such as proanthocyanidins, alkaloids, and terpenoids[38-40]. This study showed that the extract of *H. phlomoides* paralyzed and killed the parasites. Alkaloids, terpenoids, and phenolic compounds were identified in the phytochemical investigation, and these may be responsible for the anthelmintic effects of the crude extract.

CONCLUSION

The current study reveals that the *H. phlomoides* crude extract is enhanced with analgesic, antiinflammatory, laxative, and anthelmintic chemicals based on a variety of methodological approaches. Additional research into the isolation and characterization may aid in the identification of new bioactive molecules from natural resources.

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