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Original Research Article

In Vivo Evaluation of Analgesic Activities of *Dioscorea dumetorum* (Kunth) Pax and *Tragia benthamii* Bak

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Abstract

An analgesic is any member of the group of drugs used to achieve analgesia, relief from pain without loss of consciousness. Pain is one of the devastating health problems commonly treated with medicinal plants. *Dioscorea dumetorum* (Kunth) Pax (Family Dioscoreaceae) is one of the popular species of yam, usually found in Africa and mostly consumed in West Africa. *Tragia benthamii* Bak. is an herbaceous twining or trailing plant which belongs to the Euphobiaceae family. The plant is indigenous to Ivory Coast extending wide spread across Africa including Nigeria. This study investigated the analgesic activities of *Dioscorea dumetorum* and *Tragia benthamii* leaves' methanol extract on mice. Acetic acid-induced writhing method was engaged. Thirty-two (32) healthy and energetic mice were grouped into eight (8) of four (4) mice. Indomethacin (25 mg/kg) was administered to the positive control group, negative control group received distilled water (10 ml/kg) while each extract treatment groups received 50, 100, 200 mg/kg respectively. Analgesic activities of the plants' extract were assessed by counting the number of writhes for 30 minutes after a latency period of 5 minutes. Reduction in the number of writhes as compared to the control groups was considered as evidence for analgesic potential of the plants. In this study, the positive control (Indomethacin), *D. dumetorum* and *T. benthamii* significantly decreased the mean number of abdominal constrictions or writhes in a dose dependent manner following the order of 200>100>50 mg/kg. The result showed that the potency of the two plants' extract was superior to that of Indomethacin but *T. benthamii* (200 mg/kg) exhibited higher analgesic activity. Values of reduction time in writhing were significantly different ($P<0.05$) among the treatments. This research revealed effective potential analgesic effects of *D. dumetorum* and *T. benthamii* which could be attributed to the presence of phytochemicals in them. Therefore, further studies to explain their mechanisms of action should be conducted to aid the discovery of new therapeutic agents for the treatment of pains.

Keywords: Analgesic, Pain, *Dioscorea dumetorum*, *Tragia benthamii*, Nigeria.

INTRODUCTION

Pain is one of the most common reason people seek medical attention. It can be defined as an undesirable physical or emotional experience and classified as acute or chronic pain. Pain is complex, so there are many treatment options - medication, therapies, and mind –body techniques. Some measures can also be taken to relieve pain from injuries such as resting the area of the body where the aches and pains are being experienced, applying ice to the affected area to help relieve pain and reduce inflammation as well as taking an over-the-counter pain reliever, or analgesic drugs such as Acetaminophen, Non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen etc. Many of these drugs cause serious side effects. Studies have shown that opiates cause physical dependency, tolerance, and addiction while NSAIDs usually cause gastrointestinal disorders (Hanson, 2009). As such, research to discover other alternatives to treat pain is crucial. Medicinal herbs have been used for centuries for therapeutic purposes. World Health Organization (WHO) encourages the use of traditional medicines in health care programs in developing countries because of the great potential they hold in prevention of various diseases (Amos *et al*., 2001).

Dioscorea dumetorum (Kunth) Pax (Plate 1) (Family Dioscoreaceae) which is known as the bitter yam, cluster yam or three leaved yam (trifoliate) is one of the popular species of yam in the genius *Dioscorea*

that is usually found in Africa (Egbuonu *et al*., 2014). *D. dumetorum* is one of the important food security crops mostly consumed in West Africa and popularly known as Esuru, Kansanrogo and Una in Yoruba, Hausa, Ibo respectively in Nigeria. *Dioscorea dumetorum* is simply identifiable through its trifoliate compound leaves that usually twine clockwise unlike most yam of economic importance. The yam tuber of the two varieties (edible and wild) are processed by boiling; though, in case of wild variety, the tubers are detoxified by slicing and soaking, boiling; often with inclusion of salt or the sliced tuber is tied in a jute sack and placed in running water for three days to eliminate the toxic and bitter compounds that are believed to be lethal to human health (Alozie *et al*., 2009). The edible kinds are cultivated while the non-edible kinds grow in wild and are not usually safe to eat. However, the non-edibles are highly exploited in traditional medicine for treatment of some illnesses such as diabetes mellitus, schistosomiasis, rheumatoid, arthritis, stomach pain, menstrual disorders, jaundice, malaria, as a topical anesthetic and also applied to suppurating abscesses (Ogbunugafor *et al*., 2014; Sonibare *et al*., 2012; and Fasanu *et al*., 2013). *Dioscorea* dumetorum is known to contain a good quantity of bioactive compounds such as phenols, alkaloids, tannins, flavonoids, saponins, glycoside steroids, anthraquinones, etc. (Alamu *et al*., 2014; Price *et al*., 2017). *Tragia benthamii* Bak. (Plate 2) (Family Euphorbiaceae) is a perennial, densely hispid-pubescent herb, with scattered, stinging hairs. The stem is elongate, slender, and twinning. Leaves are simple, alternate, serrate, stipulate, 2.5–12.5 cm long, 2–4.5 cm broad, densely hispid-pubescent. It is a weed and therefore propagates easily and survives in harsh weather conditions. Although, this plant has been in use for thousands of years, at present, the public is not fully aware of the medicinal value, and since it causes a severe stinging effect when touched, the plant is being extensively destroyed. Due to the destruction of the plant, it is restricted to certain districts of the country. In folk medicine, *T. benthamii* leaf is being used to treat inflammation, wounds, eczema, scabies, skin infections and can be used as insect repellents. It has also been found to be effective in treating pain and bronchitis (Kirtikar and Basu, 1987). *T. benthamii* root has been traditionally used for the treatment of high fever. It reduces the elevated body temperature to normal by its diaphoretic action. The whole plant may likewise be utilized as a cardiotonic and for the treatment of Elephant's skin diseases and can as well be used as a mouth wash to cleanse oral cavity and to eliminate toxins from the body. Dash *et al.*, (2000) revealed the presence of alkaloids, carbohydrates, proteins, tannins, flavonoids, sterols and saponins in the different extracts of *T. benthamii*. The objective of this study was to assess the analgesic activities of the leaves of *Dioscorea dumetorum* and *Tragia benthamii* methanol extract on mice using Acetic-acid writhing method.

Plate 1: *Dioscorea dumetorum* (Kunth) Pax

Plate 2: *Tragia benthamii* Bak.

MATERIALS AND METHODS

Preparation of plants' extract

Fresh leaves of *Dioscorea dumetorum* were collected at Erúsú Akoko, Ondo State while *Trigia benthamii* leaves were collected from the wild in Akungba Akoko Ondo State, Nigeria. The plants were identified at the Department of Plant Science and Biotechnology Herbarium, AAUA where the voucher specimen was deposited for future reference. The leaves were air-dried in the shade and powdered mechanically using electric blender. Each powdered sample was macerated with methanol for 7 days, filtered with a muslin cloth and concentrated to complete dryness at room temperature.

Experimental animals

Thirty-two (32) healthy and energetic female mice weighing between 20 - 40 g were obtained from Akungba Akoko, Ondo State, Nigeria and housed in Plant Science and Biotechnology animal house, Adekunle Ajasin University, Akungba Akoko, Ondo State, Nigeria. They were acclimatized for two weeks before the initiation of the experiment and kept in cages under appropriate environmental condition of temperature, relative humidity and 12 hours light/dark/cycle. The animals were carefully fed ad *libitum* each day with standard diet (pellets) and water which was handled in concession with National Institute of Health guidance (NIH publication, 1985).

Acetic-acid writhing test method

The study was conducted using the method of Koster *et al.*, (1959), as modified by Dambisya and Lee (1999). Before the commencement of the experiment, all the animals were fasted for 12 hours and randomly divided into eight groups of four mice each: group 1 was assigned as negative control and was treated with distilled water (10 ml/kg), group 2 served as positive control and was treated with standard drug, Indomethacin, 25 mg/kg), groups 3-8 were assigned as test groups for both *Dioscorea dumetorum* and *Tragia benthamii* methanol extract while each plant extract received dosages of 50, 100, 200 mg/kg respectively orally. Acetic acid (1% v/v) (10 ml/kg, orally) was used to induce pain in groups 2-8 of the animals, 30 mins after receiving the treatments. Analgesic activity of the extract was assessed by counting the number of writhes (contraction of the abdominal muscles and the stretching of the hind limbs) for 30 mins after a latency period of 5 mins. The reduction in the number of writhes as compared to the negative control group was considered as evidence for analgesic potential of the extract. Each group's writhing reduction time was observed and calculated to assess the degree of analgesia.

$$\text{Analgesic activity} = \frac{\text{Mean writhing count (control - treated)}}{\text{Mean writhing count (control)}}$$

Statistical Analysis

The data collected was subjected to Analysis of Variance (ANOVA) using Statistical Package for Social Science (SPSS) software version 22 to generate the mean and standard error. Mean generated were separated and compared by Duncan's New Multiple Test (DMRT) and the results were considered significant at $P < 0.05$.

RESULTS

Effect of the analgesic activities of *D. dumetorum* and *T. benthamii* on reduction time of writhes count is shown in Table 1. The plants demonstrated dose dependent activity pattern when compared to negative control. In *Dioscorea dumetorum* methanol treated groups, lowest number of writhes count was observed in 200 mg/kg as well as in *Tragia benthamii* treated groups followed by 100 and 50 mg/kg in both plants. The plants' extract were able to produce lesser number of writhes count than the standard drug, Indomethacin. The overall results showed *Tragia benthamii* (200 mg/kg) to be the most potent. Values of reduction time in writhing were significantly different ($P < 0.05$) among the treatments.

Table 1: Effect of the Analgesic Activities of *Dioscorea dumetorum* and *Tragia benthamii* on Reduction Time of Writhes Count

S/N	Treatment/ Concentration	Mean Number of Writhing ± SEM
	DW 10 ml/kg	0.00 ± 0.00^{a}
	IM, 25 mg/kg)	40.33 ± 1.45^{d}
	DD 50 mg/kg	33.00 ± 1.15^{c}
	DD 100 mg/kg	32.33 ± 1.45^{c}
	DD 200 mg/kg	30.00 ± 1.15^{c}
	TB 50 mg/kg	52.00 ± 0.58^{e}
	TB 100 mg/kg	41.30 ± 0.88^{d}
	TB 200 mg/kg	20.33 ± 0.80^{b}

Data are represented as mean ± standard error. Mean values with the same superscript alphabets in the rows are not significantly different from each other ($P>0.05$).

Key: DW= Distilled water, IM= Indomethacin, DD= *Dioscorea dumetorum* methanol extract, TB= *Tragia benthamii* methanol extract.

DISCUSSION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (Bauman, 2002). Pain is a warning signal. Primarily protective in nature, but causes discomfort and suffering and usually initiated by noxious stimuli and transmitted over specialized neural networks to the central nervous system. Untreated and persistently prolonged pain is the most pervasive disorder that results to both physical damage and psychological disorder (Henschke *et al.*, 2015). Analgesics are drugs used to treat or reduce pain and the classical analgesic drugs notably opiates and non-steroidal anti-inflammatory drugs have their origin in natural products but many synthetic compounds that act by the same mechanism have been developed and are associated

with serious adverse effects such as ulceration, gastrointestinal bleeding, respiratory distress, drowsiness, nausea, etc (Mate *et al.,* 2008). Based on these, there is need to the search for bioactive compounds from natural products especially from medicinal plants for use as alternative analgesics with little or no side effects.

In this study, analgesic activities of mice induced with acetic acid and treated with *D. dumetorum* and *T. benthamii* methanol extract were evaluated. Acetic acid-induced writhing reflex is a model of visceral pain which is highly useful for screening analgesic drugs and several chemicals such as phenylquinine in laboratory animals (Hasan *et al.,* 2010). Acetic acid produces writhing reflex in animals by activating the chemo sensitive nociceptors (Onasanwo and Elegbe, 2006). Also, it has been noted that the level of analgesia in acetic acid-induced models is indicated by the percent reduction in the number of abdominal constrictions (Marchioro *et al.,* 2005). In this study, the positive control (Indomethacin), *D. dumetorum* and *T. benthamii* significantly decreased the mean number of abdominal constrictions or writhes in a dose dependent manner following the order of 200>100>50 mg/kg. The result showed that the potency of the two plants' extract was superior to that of Indomethacin but *T. benthamii* (200 mg/kg) exhibited higher analgesic activity. Acetic acid-induced writhing model produces pain sensation by triggering inflammatory response and such pain stimulus leads to release of arachidonic acid from tissue. The analgesic effect of the plants observed in this study may be mediated through peripheral pain mechanism and or through suppression of prostaglandin pathway since it has been observed that any agent that decreases the number of writhing will demonstrate analgesia preferably by inhibition of prostaglandin synthesis, a peripheral mechanism of pain inhibition (Ferdous *et al.,* 2008). This observation was in line with report of Ukwueze *et al.,* (2015). Similar result was also reported by Ezeja *et al.* (2011). Active substances against pain may either interfere with pain mediator systems or act on the central nervous system (CNS) by blocking the pain influx transmission (Anaga and Onehi, 2010).

CONCLUSION

This research revealed effective potential analgesic effects of *D. dumetorum* and *T. benthamii* which could be attributed to the presence of phytochemicals in them. Therefore, further studies to explain their mechanisms of action should be conducted to aid the discovery of new therapeutic agents for the treatment of pains.

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