Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i5.6332

IN VIVO ANALGESIC, MUSCLE RELAXANT AND SEDATIVE EVALUATION OF CRUDE EXTRACT OF *TAXUS WALLICIANA* Zucc.

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Abstract
Traditionally, *Taxus walliciana* has been used to treat various ailments, including cancer, pain, convulsions, and fever. This study investigated the analgesic, muscle relaxant, and sedative effects of the crude extract of the whole *Taxus walliciana* plant. The results showed a significant ($p < 0.001$) analgesic effect, with 88% attenuation of writhing. However, the extract did not exhibit central analgesic activity in the hot plate model. A short-term muscle relaxant effect was observed, with 33% and 75% efficacy in the traction and inclined plane models, respectively. No sedative effect was noted. In conclusion, the crude extract of *Taxus walliciana* demonstrates analgesic and muscle relaxant properties, warranting further investigation into its potential therapeutic applications.

Keywords: *Taxus walliciana,* analgesic, muscle relaxant, sedation

1.0 Introduction

According to the WHO (World Health Organization), plants of therapeutic value will be the key source to acquire a series of drugs. Traditional medicines are used by around 80% of individuals from underdeveloped countries, which comprise compounds attained from medicinal plants [1-4]. Since 19th century, the characterization and isolation of plants have led to medicinally significant classes of different bioactive constituents [5-6]. Over the centuries, phytopharmaceuticals have been utilized by various communities worldwide [7]. In Pakistan, local communities have long relied on medicinal plants as a primary component of their healthcare system, using them to treat a wide range of diseases [8-9]. This practice, known as Hikmat or Tabib, is well-established in the country. Approximately 600 to 1,000 medicinal plants are used in treating various pathological conditions by over 40,000 registered[10], as well as many unregistered, Hakims or Tabibs. However, this practice is based on experiential knowledge rather than scientific evidence and therefore requires proper scientific validation. From the very start of human life on earth human being have started using plants, as these plants are the chief source of bioactive molecules that are used to cure various diseases in humans such as infections caused by microorganisms, healing of wounds, and many others. Plants have been used as medicines from as early as 1770 BC reported by Babylonian civilization.[11] Such medicinally valuable plants have been digging out from the pyramids of Gaza. These specimens are preserved in the museum of Cairo. our life span during 20th century has been doubled with the help of plants and their secondary metabolites, revolutionized medicines, and reduced pain. The involvement to the

natural product chemistry is the conformational analysis described by the Derk Berton and used for the structural determination of the complicated molecules [12]. Traditionally medicinal plants has higher values in health care purposes as compared to novel drugs, an ample amount of allopathic medicines are synthesized from these medicinally important plant extracts [13].

Taxus wallichiana belongs to the Taxaceae family that is mostly recognized as the Himlayan yew. Locally it is called Burmi. It is extensively distributed in India, Pakistan, and China and is mostly used in folk medicines. Taxol and associated bioactive toxoids have been listed from the many species of this genus, including *Taxus wallichaina. T. wallichiana* is an evergreen, medium-sized, coniferous tree which can grow as tall as 20 m. Its shoots in first are green which changes color after three to four years to brown. The leaves of the plant are flat, thin, and slightly sickle-shaped, having lengths ranging from 1.5-2.7 cm and with 2mm breadth, having a soft apex. Leaves are settled spirally on the shoots and warped at the base to appear in two horizontal positions all excluding the straight main shoots. It has female and male cones on different plants. The seed contains single dark brown seed with a length of 7mm[14]. The plants of the Taxus genus are reported to have antitumor agents and have anticancer properties. The plant also reportedly has other pharmacological actions such as, anti-allergic [15] , Immunomodulatory [16] , anti-inflammatory, antinociceptive [17] , antiplatelet, vasorelaxant, and antiosteoporosis activities [18] . in the current studies, the whole plant was subjected to analgesic effect in animals Molde.

2.0 Materials and Methods

Most of the chemicals used in this study were of analytical grade such as Diclofenac sodium (Asian Continental (Pvt) Ltd Pakistan), acetic acid, Brewer's yeast (Merck, Germany), carrageenan (Sigma Lambda, USA), Diazepam (Martin Dow Ltd. Pakistan) and Tramadol® (Searle Pakistan Ltd.) were used. For all experiments, a control solution of sterile normal saline was used, and the methanolic extract was dissolved in normal saline to prepare the test solution.

2.2Animals

BALB/c mice were bought from the veterinary research institute in Peshawar, Pakistan. The animals were shifted to the animal house of the Department of Pharmacy, AWKUM Pakistan. Only healthy animals were allowed to be used in experiments. The animals were provided with standard laboratory food and fresh water *ad libitum*. The study was approved by the ethical committee of the Pharmacy Department at AWKUM.

2.3 Acute toxicity

The extract was tested for acute toxicity of *Taxus wallichiana.* BALB/c mice (n = 6) at various doses, such as 500, 1000, 2000 mg/kg, p.o. as well and the control group was given a saline (10ml/kg). The animals were observed for 4 h after dose administration for any gross behavioral changes After a 24-hour period, the number of mortalities was determined and recorded.[19]

2.4 Analgesic effect

2.4.1 Acetic acid-induced worthing's

Animals were classified as negative control (treated with 10 ml/kg, IP), positive control (treated with diclofenac, 10 mg/kg, IP) and tested groups (treated with extract). After 30 min of these treatments each animal was injected with 1% acetic acid for induction of abdominal wriths. [19] After 10 min of acetic acid treatment, each animal was observed for 10 min for several abdominal contractions. The following formula was used to calculate the percent analgesic effect.

$$\% \text{ effect} . = \frac{Cw-Tw}{Cw} X100$$

Where Cw= adnominal writhes of negative control and Tw= abdominal writs of tested groups.

2.4.2 Hot plat

The animals were classified as above and negative control animals were administered with Normal Saline, the positive control animals were treated with Tramadol and the tested animals were treated with extract. After 30 min of these treatments each animals was allowed to stay on the hot plate and the time duration was noted (latency time in seconds). The latency time was periodically noted after 30, 60, 90 and 120 min. The percentage effect was calculated using the formula in literature.[19]

2.5 Muscle relaxant

The muscle co-ordination effect was evaluated in the following models.

2.5.1 Tractions test

In this procedure, a metal wire coated with rubber was securely supported at both ends by stands, approximately 60 cm above the laboratory bench. The animals were divided into groups (n = 6). Group I, serving as the negative control, was treated with distilled water (10 mL/kg, i.p.), while Group II, the positive control, was treated with diazepam (1.0 mg/kg, i.p.). The remaining groups were treated with the extract. Thirty minutes after these treatments, each animal were suspended upside down by their hind legs from a wire, and the duration of hanging was measured for a maximum of 5 seconds. If an animal failed to hang for the full 5 seconds, it was considered an indication of muscle relaxant activity [20].

2.6 Sedative

The open field test was employed to evaluate the sedative effects of a drug. The testing apparatus comprised a circular white wooden area with a diameter of 150 cm, surrounded by stainless steel walls and divided into 19 squares with black lines. This setup was located in a room insulated from light and sound. Prior to the experiment, the animals were acclimated for one hour under red light (provided by a 40-watt red bulb) with free access to food and water. For controls, normal saline (10 ml/kg) was used as a negative control, and diazepam (0.5 mg/kg) served as the reference drug. Other groups received crude extract and fractions of *Taxus wallichiana* extract. After a 30-minute period, each animal was placed in the center of the box, and the number of lines crossed by each mouse was recorded [21].

2.7 Statistical analysis

The graph Pad prism was used for statistical analysis. One way ANONA and two WAY ANOVA were used as statistical tests.

3.0 Results

3.1 Acute toxicity

The extract was found safe at all tested doses and no mortality was observed.

3. 2 Analgesic effect

The analgesic effect in the acetic acid-induced writhing model is presented in **Table 1**. The significant ($p<0.001$) analgesic effect was noted against all tested doses. The maximum % inhibition was 88.80 and 88.81 at the tested doses of 0.2 and 0.4 ML respectively as shown in **Fig. 1**. While no analgesic effect was observed in the hot plate test.

Table 1. analgesic effect of whole plant of *Taxus walliciana* in acetic acid-induced model.

Analgesic Activity (Writhing)			
SAMPLE	**DOSE**	**WRITHS**	**%**
NS	10 ML	110.20 ±1.60	
DICLO	10 MG	8.10±1.20***	92.72
EXTRACT	0.1 ML	20.40±1.30***	81.81
	0.2 ML	13.20±1.20***	88.18
	0.4 ML	12.30±1.40***	88.80

The data were presented as Mean ±SEM. ONE WAY ANONA was applied for determination of the level of significance. P<0.05*, P<0.01**, P<0.001***

3.3 Muscle relaxant effect

In both of the tested models a the muscle co-ordination effect was noticed only after 30 min while no muscle relaxant effect was observed after 60 and 90 min. the extract exhibited 33 % effect in traction model and 75% effect in inclined plane model as shown in **Table 2**.

Table 2. The muscle relaxant effect whole plant of *Taxus walliciana*

Muscle Relaxant							
Sample	**DOSE**	**Traction %**			**Inclined Plan %**		
		30	**60**	**90 MIN**	**30**	**60**	**90 MIN**
Normal Saline	10 mL	0±0.00	0±0.00	0±0.00	0±0.00	0±0.00	0±0.00
DIAZEPAM	1 mg	100±0.00	100±0.00	100±0.00	100±0.00	100±0.00	100±0.00
Plant Extract	0.22 ML (of 1 % Solution)	33.21±1.40	0±0.00	0±0.00	75.30 ±1.30	0±0.00	0±0.00

3.4 Sedative effect

The sedative effect of the crude extract is presented in **Table 3**. No sedative effect was observed at any dose.

Table 3. The Sedative effect whole plant of *Taxus walliciana*

Sedative activity		
Treatment	**Dose**	**Number of lines crossed in 10 minutes**
Normal Saline	10mL/Kg	170.30±0.33
Plant Extract	0.3 mg /Kg	190.45±0.40
	0.4 mg/Kg	192.60±1.20
	0.5 mg/Kg	189.30±0.90
Diazepam	0.5 mg/Kg	2.70±0.50***

4.0 Discussion

Medicinal plants are the main source of therapeutic agents for the treatment and management of various ailments [22-23]. The practice of natural products as therapeutic agents is going on around the globe in various forms. Due to the best safety profile and affordability of these natural products the consumption of these products as alternative medicines is increasing day to day [23-25]. Even in the current modern era, the concept of nutraceuticals is also a good business.[26] The awareness of the side effects of available synthetic drugs is the main reason for poor patient compliance, especially that of painkillers. The patient is reluctant to use the painkiller due to the fear of peptic ulcer. In comparison to the synthetic drugs causing peptic ulcer the trend of this side effect is low in natural medicines. Therefore, the search for safe, effective, and economical painkillers is of utmost essential to maximize the patient compliance concerning the use of analgesics for various pathological and non-pathological conditions. [19]

The current studies are subjected to *Taxus walliciana* for analgesic and muscle relaxant effects. The significant analgesic effect of this extract indicates that the plant might be the inhibitor of local pain receptors or might be the antagonist of the COX. COX is responsible for prostaglandin production which later creates pain, inflammation, and pyrexia. The ethnomedicinal use of this plant as an antipyretic supports the suggestion of COX inhibitory aspects. The mild muscle co-ordination effect supports the anticonvulsant effect of this plant.

However, further mechanistic molecular level studies are needed to confirm the mechanism and use of this plant. The well knows use of this plant in oncology is also best for our studies because of the painful condition of cancer.

5.0 Conclusion

The study evaluated the effects of the crude extract of the whole plant of *Taxus wallichiana* in animal models, focusing on its analgesic, muscle relaxant, and sedative properties. The findings indicate that *Taxus wallichiana* exhibits significant peripheral analgesic effects. However, the extract did not show central analgesic activity in the hot plate model. Additionally, the extract demonstrated muscle relaxant effects, with 33% effectiveness in the traction test and 75% in the inclined plane model, although these effects were of short duration. No sedative effects were observed. So, the crude extract of *Taxus wallichiana* possesses notable analgesic and muscle relaxant properties, supporting its traditional use for pain relief and muscle relaxation. Further studies are recommended to isolate and identify the active compounds responsible for these effects and to explore their potential therapeutic applications.

Acknowledgment

All the authors express gratitude to the Department of Chemistry, Department of Pharmacy, University of Swabi, Pakistan and Department of Pharmacy AWKUM Pakistan for providing research facilities.

Conflict of Interests

Authors declared no conflict of interests.

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