

## Analgesic activity of *Terminalia bellerica* fruit pulp aqueous extract by using acetic acid induced writhing test in Swiss albino mice by peripheral mechanism

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### Abstract

**Objective:** To evaluate analgesic activity of *Terminalia bellerica* fruit pulp aqueous extract by acetic acid induced writhing reflex test in Swiss albino mice by peripheral mechanism.

**Materials and Methods:** Albino mice of Swiss strain (Male / Female-equal number), were selected for the study and each mouse weighed about 15-30gms. Five experimental groups made assigned as Control, Standard and three groups of test drugs at different doses, and the doses were Gum acacia (1%), 10ml/kg, Diclofenac sodium (30mg/kg), *Terminalia bellerica* 9, 18 and 36 mg/kg respectively. All the drugs were administered orally one hour before commencing the experiment followed by injecting 0.1 ml of 0.6% acetic acid intraperitoneally and writhing reflex was observed for next five minutes. Observations recorded as mean  $\pm$  SD. Results obtained were analyzed by using ANOVA (one-way) statistical test followed by Dunnet's multiple comparison test and if p value <0.05 was considered statistically significant.

**Results:** Our study reveals that aqueous extract of *Terminalia bellerica* fruit pulp in the dose of 9mg/kg ( $4.83 \pm 1.47 = p < 0.045$ ), 18mg/kg ( $4.33 \pm 2.42 = p < 0.024$ ) and 36mg/kg ( $4.17 \pm 2.40 = p < 0.019$ ) significantly decreased the total number of writhing reflex at the doses (9, 18 & 36 mg/kg) by acetic acid induced writhing reflex test in Swiss Albino mice when compared to control.

**Conclusion:** Aqueous extract of *Terminalia bellerica* fruit pulp exhibited peripheral action in all the dose of 9, 18 and 36 mg/kg by acetic acid induced writhing reflex test in Swiss albino mice.

**Keywords:** Aqueous extract, Fruit pulp, Peripheral analgesic activity, *Terminalia bellerica*, Writhing test.

### Introduction

Humans usually suffer from algesia, pyrexia and inflammation in daily life for various reasons. Many drugs are existing in the market and they are also available as over the counter (OTC) drugs but they generally carry the risk of causing adverse drug reactions (ADRs) which may be as mild as nausea and in severity may even cause death. One of the major adverse effect of the prototype (Aspirin) non-steroidal anti-inflammatory drug (NSAID), is gastric ulcer, bleeding from stomach etc. Moreover, in children and in adolescent, it is no longer preferred as it carries the risk of causing Reye's syndrome especially in case of children suffering from viral hepatitis.<sup>1</sup>

Selective COX 2 inhibitors have advantages over conventional NSAIDs, it is known for its adverse effects on cardiovascular system and moreover many drugs in this group have been already withdrawn from the market. Nimuselide even though initially has shown promising results, but has been banned in many countries due to its liver toxicity effects. On the contrary, paracetamol had very efficacious analgesic and antipyretic effect but has very poor anti-inflammatory activity thus exhibiting its drawbacks and also not safe in overdose.<sup>2</sup> Anti-inflammatory activity of corticosteroids is well known, but are devoid of analgesic and also antipyretic activity and moreover they carry their own adverse effects in overdose and especially on long term use. They also delay the wound healing process in the body.<sup>3</sup>

Opioids are known to act by central mechanism but is devoid of anti-inflammatory and antipyretic effect and moreover carries high risk of abuse and dependence liability.<sup>4</sup> Several evidences suggest the role of herbal medicine in treatment of diseases and Ayurveda stands as a back bone for the rationalized treatment in Indian system medicine<sup>5</sup>. From many centuries, plants and their products or byproducts are known to possess analgesic, anti-inflammatory and antipyretic affects.<sup>6</sup>

*Terminalia bellerica* is well mentioned in Indian system of medicine. It is a tree and its fruit pulp is mentioned to be having many therapeutic uses in the management of pain, diarrhea, hypertension, infections, spasms, asthma and other conditions. As its analgesic activity has been formerly reported in many studies, but its effect is on peripheral or central was not has not been clearly mentioned. In view of this, the following study has been undertaken to find its analgesic activity of *Terminalia bellerica* fruit pulp aqueous extract by using acetic acid induced writhing reflex test in Swiss albino mice by peripheral mechanism.

### Materials and Methods

Institutional animal ethical committee permission was obtained from A.J. Institute of Medical Sciences and Research Centre, Kuntikana, Mangalore, Karnataka, India wide ref.no. 1075/ac/07/CPCSEA dated 27/07/07. Albino mice of Swiss strain (Male / Female-equal number), were selected for the study and each mouse weighed about 15-30gms. Five

experimental groups were assigned as Control, Standard and three groups of test drugs at different doses, and the doses were Gum acacia (1%), 10ml/kg, Diclofenac sodium (30mg/kg), *Terminalia bellerica* 9, 18 and 36 mg/kg respectively. All the drugs were administered orally one hour before commencing the experiment followed by injecting 0.1 ml of 0.6% acetic acid intraperitoneally and writhing reflex was observed for next five minutes. A writhe was taken in consideration when animal showed contraction of abdomen with simultaneous stretching of at least one hind limb. The formula for computing percent inhibition is: average writhes in the control group minus writhes in the drug group divided by writhes in the control

group times 100%. The total time period with the greatest percent of inhibition is considered the peak time. A dose range is reserved for interesting compounds or those which inhibit writhing more than 70%. Compounds with less than 70% inhibition are considered to have minimal activity.

### Statistics Analysis

Observations were recorded as mean  $\pm$  SD. Results obtained were recorded by using ANOVA (one-way) statistical test followed by Dunnet's multiple comparison test and if p value was found  $<0.05$  then it was considered statistically significant.

## Results and Discussion

**Table 1: Peripheral Analgesic Activity of *Terminalia bellerica* aqueous extract by Acetic Acid Induced Writhing Reflex Test in Swiss Albino Mice**

Groups	Drug / Dose	Writhing Reflex (mean $\pm$ SD)
I	Control (1% gum acacia (10 ml/kg), p.o)	10.6 $\pm$ 1.17
II	Standard (Diclofenac (30 mg/kg) p.o)	4.92 $\pm$ 0.01***
III	<i>Terminalia bellerica</i> 9mg/kg, p.o	4.83 $\pm$ 1.47***
IV	<i>Terminalia bellerica</i> 18mg/kg, p.o	4.33 $\pm$ 2.42***
V	<i>Terminalia bellerica</i> 36mg/kg, p.o	
Statistical method-ANOVA, post hoc - Dunnet's Multiple Comparison test. Mean $\pm$ SD are observations. *p>0.05-Not Significant, **p<0.05-Significant, ***p<0.01-Highly significant		

*Terminalia bellerica* fruit pulp aqueous extract has shown analgesic effect in animal model of acetic acid induced writhing reflex test in Swiss albino mice with a p value of  $<0.01$  exhibiting its high significant result compared to control in ANOVA test at all the tested doses (Table 1). However, this study has shown a peripheral analgesic activity, but whether central component is involved in it for its action has to be screened by comparing with a standard opioid compound. Moreover, the molecular mechanism of action of its peripheral analgesic activity has to be evaluated by suitable method in a larger sample in different models as well

### Conclusion

*Terminalia bellerica* fruit pulp aqueous extract has exhibited a highly significant peripheral analgesic action.

### References

1. Macdonald S "Aspirin use to be banned in under 16 year olds". BMJ. 2002; 325 (7371):988.
2. Kearney P M, Baigent C, Godwin J, Halls H, Emberson J R, Patrono C. "Do selective cyclo-oxygenase-2 inhibitors and traditional non-steroidal anti-inflammatory drugs

increase the risk of atherothrombosis? Meta-analysis of randomized trials" BMJ (Clinical research ed.) BMJ;332(7553):1302-1308,

3. Mehlisch DR. "The efficacy of combination analgesic therapy in relieving dental pain". Journal of American Dental Association. 2002 133(7):861-71.
4. Janssen P, Niemegeers CJE, Dony JGH. The inhibitory effect of fentanyl and other morphine like analgesics on the warm water induced tail withdrawal reflex in rats. *Arzneim Forsch.* 1963;13:502-507
5. Balunas MJ, Kinghorn. Drug discovery from medicinal plants. *Life Sci*, 78, 2005,431-44.
6. B.K. Nanda, J. Jena, B.Rath, B.R.Behera. Analgesic and Antipyretic activity of whole parts of *Sphaeranthus indicus* Linn. *Journal of Chemical and Pharmaceutical Research*, 1 (1), 2009, 207- 212.