ABSTRACT

Background: *Tithonia diversifolia* is the one kind of plant that is widely used in the traditional medicine. *Tithonia diversifolia* is provend to inhibits cell proliferation of fibroblast keloid, inhibits accumulation collagen *in vitro* and decrease the index of scar hyperthrophy *in vivo*.

Objectives: The aim of this study was to evaluate the toxicity of *Tithonia diversifolia* in male and female Wistar rats during 90-days observation period.

Methods: This was an experimental post test only controlled group design used total one hundred rats, two months old male and female Wistar rats with a body weight ranging from 200-300g where purchased from the Laboratory of Pharmacy UGM. Wistar rats were divided into 5 groups randomly, give *T. diversifolia* dosage 2%, 10%, 25%, satellite group and control group. Then, analysis NOAEL done based on the clinical observations, haematology, clinical biochemistry, and histopathology of skin, liver and kidney.

Results: There was no obvious symptom on the clinical observations. In the repeated dose 90-day dermal toxicity study, the administration of 2%, 10%, and 25% *Tithonia diversifolia* gel formulation revealed no significant difference ($p>0.05$) haematological and biochemical parameters, except a significant differences was found increase neutrophils dose 25% of male Wistar rats and increase hematocrit dose 10% and 25% of female Wistar rats, and increase SGOT of male and female Wistar rats, however the increasing still in normal level. The skin, liver, and kidneys of male and female Wistar rats in the all of groups showed normal structures.

Summary: *Tithonia diversifolia* gel formulation applied toward Wistar rats for 90 days does not cause any apparent *in vivo* toxicity by observation NOAEL (*No Observe Adverse Effect Level),* it also does not give effect to haematology, liver and kidney function, and not cause organ damage or lesions on the skin, liver, and kidney and reveals a normal morphology similar to the control group.

Keyword: *Tithonia diversifolia,* gel preparation, subchronic dermal toxicity, NOAEL