DETERMINATION OF LD₅₀ OF ORAL GENTAMICIN-NIGELLA SATIVA EMULSION (GNE) IN RABBIT.

Muhammad Hamzah Ahmad Halmi¹*, Mohd Affendi Mohd Shafri¹, Farahidah Mohamed³, Nazri Mohd Yusof²

¹Department of Biomedical Science, Faculty of Allied Health Sciences, International Islamic University Malaysia (IIUM), 25200 Kuantan, Malaysia.
²Department of Orthopaedic, Faculty of Medicine, International Islamic University Malaysia (IIUM), 25200 Kuantan, Malaysia.
³Department of Pharmaceutical Technology, Faculty of Pharmacy, International Islamic University Malaysia (IIUM), 25200 Kuantan, Malaysia.

*Corresponding author email: hamzahhalmi@gmail.com

ABSTRACT

Antibiotic resistance has been recognized by the World Health Organization (WHO) as among the three major threats to global health. A combinational approach can provide an opportunity for a synergistic interaction between plant extract and conventional antibiotics to combat antibacterial resistant. A stable emulsion which contains Nigella sativa oil (NSO) and gentamicin has been formulated as an alternative antimicrobial therapy to treat Staphylococcus aureus osteomyelitis. Previously, gentamicin and N. sativa emulsion (GNE) was reported to be effective against Staphylococcus aureus and capable to impede the ability of bacteria to form biofilm based on Disc Diffusion assay and Biofilm Inhibition Formation. The present study was to assess the toxicological profile of GNE by acute oral toxicity in rabbits by the method of OECD guidelines 425. GNE was administered to rabbits by force-feeding procedure with the start dose of 267 mg gentamicin/kg b. wt. and progressed to dose 854 mg gentamicin/kg b. wt. for the next rabbit. The test was stopped after five reversals occurred in six consecutive rabbits tested. Blood samples were collected 2 hours after dosing for blood profile analysis and gentamicin detection. The surviving rabbits were observed for 14 days for any signs of toxicity and delayed death. An oral dose of GNE, caused immediate agitation and behavioural perturbation with temporary writhing, followed by quiet attitude period and sedation. At a higher dose, the serum gentamicin concentration was detected at 10 µg/mL, and all of the rabbits died within the 12-hour overnight period. At the lower dose, all of the rabbits survived, and the serum gentamicin concentration was detected at 1.79 µg/mL. However, minor alteration to body weight and reduced water and food intake were observed in the surviving rabbits. The surviving rabbits quickly recovered their normal activity and growth after a period ranging from 1 to 2 weeks afterwards. The LD₅₀ in rabbits for oral GNE was determined to be 477.5 mg gentamicin/kg b. wt. The trace of gentamicin in the blood serum has shown some evidence of the absorption of gentamicin through the gastrointestinal tract. Oral GNE administration did cause acute toxicity effect and death in rabbits at 854 mg gentamicin/kg b. wt.

Keywords: osteomyelitis, GNE; Staphylococcus aureus, LD₅₀, antibiotics.

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