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Evaluation of sesamol-induced histopathological, biochemical, haematological and genomic alteration after acute oral toxicity in female C57BL/6 mice

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ABSTRACT

The objective of this study was to evaluate organ-wise toxicological effects of sesamol and determine the LD_{50} cut-off value and GHS category following acute oral toxicity method OECD 423. An acute oral toxicity study was carried out in female C57BL/6 mice. Observations for physical behaviour and measurements on haematology, biochemistry, histology of vital organs were performed. In addition, genotoxicity assessment using comet and micronuclei assays was also performed. Acute toxicological effects were observed at 2000 mg/kg, while no adverse effects observed at 300 mg/kg. The effects of 2000 mg/kg were manifested as severe histopathological changes in all organs (femur, spleen, gastrointestine, lungs, heart, kidney, liver, stomach and brain) and excessive DNA strands breaks occurred in femoral bone marrow cells and splenocytes. A single dose of sesamol (2000 mg/kg, body weight) caused the death of two mice (out of three) within 2 h. Hence, sesamol is in GHS category 4 (>300–2000) with LD_{50} cut-off value of 500 mg/kg body weight. In contrast, this study is correlated with the obtained GHS category 4 and LD_{50} cut-off value 580 mg/kg body weight by ProTox. In conclusions, the present study has classified sesamol toxicity and assessed organ-wise acute oral toxicity of sesamol in female C57BL/6 mice. Therefore, these findings may be useful for the selection of dosages for further pre-clinical evaluation and potential drug developmental of sesamol.

1. Introduction

Oxidative stresses have been implicated as causative agents in various disorders such as hepatic fibrosis [34], pulmonary inflammation [33], cardio vascular disorders [8], diabetic complication [13], renal disease [3,38,42], cancer radiation syndrome [43], several neurodegenerative disorders [45] and the aging process [12]. Thus, antioxidants that scavenge free radicals and reactive oxygen species may be considerable potential in ameliorating these disease processes. In the past few years, natural and endogenous antioxidants have created considerable research interest for prevention or amelioration of these diseases.

Sesamol (3,4-methylenedioxyphenol), is an important constituent of sesame oilseed and is well-known for its nutritional and medicinal value. It is used in ancient Chinese and Indian ayurvedic medicine for various health problems. The antioxidant properties have been attributed to a number of polyphenolic substances including sesamolin and sesamin [4]. Sesamol, possess good antioxidant activity due to a benzodioxole group, which is known to scavenge hydroxyl radical and also produces another antioxidant 1,2-dihydroxybenzene [23]. In a number of in-vitro and in-vivo investigations, sesamol has been documented as direct free radical scavenger and indirect antioxidant [17,18,32,35].

Sesamol is responsible for the stability of sesame oil [1], and is an efficacious potential antioxidant and free radical scavenger

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