ABSTRACT

Acetaminophen (also known as Paracetamol) is the most widely used over the counter medication during pregnancy and it ranks at the top of the list. Acetaminophen is safe and effective when we use lower dose, but excessive usage can damage liver. There is evidence that overdoses of acetaminophen during pregnancy increases the risk for adverse reproductive outcomes, e.g. spontaneous abortions, a variety of malformations, fetal distress and hepatic and renal toxicity in infants.

Liv.52 is an herbal hepatoprotective formulation known to improve the functional efficiency of the liver by promoting detoxification and thus protecting from harmful food and medication toxins, maintaining healthy levels of liver enzymes. Even though hepatoprotective effect of Liv.52 has been reported by several researchers, protective role of Liv.52 in acetaminophen induced maternal and developmental toxicity is not been tested. There is no information available regarding protection of acetaminophen induced hepatotoxicity will also protect its developmental toxic effects in a mammalian species.

The objective of this study was to assess the toxicity effect of co-administration of Liv.52 on the toxicity of Acetaminophen when administered repeatedly for 7/14 consecutive days and to evaluate the protective role of Liv.52 on acetaminophen induced effects on pregnant rats, embryo fetal developmental toxicity (teratogenicity) and lactating rats and their developing fetuses/pups when administered orally to rats from ‘0’ day of pregnancy and up to 19 day of gestation and also through weaning (PND21).

In embryogenesis study, dose-dependent decrease in maternal body weights, food intake, gravid uterine weight and male, female and total fetal weights as well as fetal length (crown–rump) were observed in dams exposed to 500 and 1000 mg/kg/day of acetaminophen. In addition, the treatment with acetaminophen at 1000 mg/kg/day resulted in decreased haematological parameters (red blood cells, hemoglobin, hematocrit and red blood cell distribution width) and decreased total number of fetuses and mean litter size. During Lactation period, dose-dependent decrease in maternal body weights and food intake in association with hepatic and renal toxicity was observed in dams exposed to 1000 mg/kg/day of acetaminophen.
These changes were associated with higher post-implantation loss, lower litter size and live birth index. At 500 mg/kg/day dose-dependent decrease in maternal body weights and food intake were observed during lactation period, but these changes were not associated with any changes in litter parameters evaluated.

The administration of Liv.52 formulation alone did not induce any toxic effects during embryogenesis and postnatal development. However, the toxicity induced by acetaminophen was attenuated completely or partially when Liv.52 at 1000 mg/kg/day was co-administered with acetaminophen at 500 mg/kg/day or 1000 mg/kg/day.

To conclude, acetaminophen can cause toxicity during embryogenesis and postnatal development at 500 or 1000 mg/kg/day. The results show that, Liv.52 an herbal formulation could attenuate acetaminophen induced toxic effects during embryogenesis and postnatal development as well as hepatotoxicity.

**KEYWORDS**

Abnormalities, Fetus, Litter, Liv.52, Acetaminophen, Toxicity, Skeletal, Prenatal, Rat