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Teratogenic effects of an extract of unripe *Mormodica charantia* fruit in rats

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Abstract: The objective of this study was to evaluate any teratogenic effects of the unripe fruit extract of *Mormodica charantia* Linn. on rats when given during mid-pregnancy (days 7–15). The extract was administered orally in two different concentrations (1 ml/100 g/day or 2 ml/100 g/day). Vitamin A (15,000 U/kg) was given intramuscularly on days 8, 9 or 10 to serve as a positive control. Several teratogenic parameters were determined in day 20 fetuses. Both doses of the extract increased the number of small-for-dates fetuses and inhibited fetal growth. The lower dose, in addition, induced a shortening of the forearm of the right forelimb of one fetus. In contrast, vitamin A treatment produced predominately dwarfed and small-for-dates fetuses with external malformations (in 10%) and skeletal abnormalities (in 20%). In adult female rats, the extract neither inhibited body weight gain, nor caused haemotoxicity (in terms of leucocyte or platelet counts or clotting time) hepatoxicity (in terms of serum SGPT activity) or nephrotoxicity (in terms of serum Na^+ and K^+ and creatinine levels) with chronic administration (for 26 weeks). We conclude that it is desirable for pregnant women to avoid heavy consumption of unripe *M. charantia* fruits in view of possible teratogenic risks.

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Keywords: developmental toxicity, fetal growth, fetal malformation, *Mormodica charantia*, pregnancy, Sri Lanka, teratogenicity

Introduction: Many people in Sri Lanka consume *Mormodica charantia* fruit as it is heavily promoted over the mass media as a safe and potent herbal remedy for diabetes. Some pregnant women, especially in villages, also consume the fruit as a vegetable curry to achieve anticipating efficient lactogenesis and sustained galactopoiesis. *M. charantia* has been claimed to be a galactogogue [1].

It is important to evaluate herbal remedies for their efficacy and safety [2]. The efficacy of *M. charantia* as an antidiabetic agent has been extensively studied both in Sri Lanka [3] and other countries [4,5]. However, its safety has not yet been extensively studied.

Recently, we investigated on the safety of *M. charantia* fruits during pregnancy using rats and found that it interrupts fetal growth if administered during mid-pregnancy [6] as reported with other clinically used antidiabetic agents [7]. Further, some antidiabetic drugs induce congenital malformations [7]. Given the widespread consumption of *M. charantia* fruits during pregnancy by Sri Lankan women, and their perceived potential for fetal growth retardation [it is imperative to assess their teratogenic potenti However, no such information has yet been published

Therefore, we initiated this study mainly to investigate t teratogenic effects of *M charantia* fruits. The dose tested h been shown to have hypoglycaemic activity in rats [3–5] a is equivalent to the dose of 100 ml recommended for use humans [8]. We also investigated the effects of the fruits some biochemical and haematological parameters in healt female rats.

Materials and methods: Fresh unripe fruits of *M. charan* were purchased from a vegetable store in Colombo, S Lanka. Their identity was authenticated by Professor R.N. Foneska, Department of Botany, University of Colombo. T fruits were washed deseeded and cut into thin slices. The were immediately minced using a Kenwood mincer and t resulting pulp squeezed through four layers of gauze.

The volume of filtrate was measured and freeze-drie using a freeze drier (Model LFD-600 EC, Laytant Li Science, Tokyo, Japan). When required the freeze-dri extracts were macerated in a porcelain mortar and reconst tuted in distilled water (DW) to the original volum 1 ml/100 g body weight and 2 ml/100 g body weight w orally administered to rats.

Healthy adult Sprague-Dawley rats (males weighi 200–250 g and females weighing 175–200 g) from our ow colony were used. They were kept in a well-ventilated an mal house under standardized conditions (temperatu 28–31 °C; photoperiod: approximately 12 h natural light an 12 h dark) and with free access to pelleted food (Oils an Fats Corp., Seeduwa, Sri Lanka) and tap water.

Pro-oestrous rats ($n = 24$) were selected by vaginal smea ing and individually paired with a male rat of proven ferti ity (between 17.00 and 18.00 h). Successful matings we confirmed by the presence of sperms in vaginal smears th following morning (between 8.00 and 9.00 h). This was de ignated as day 1 of presumed pregnancy.

Eighteen, day 7 pregnant rats were randomly divided int three groups and orally treated (8.00 – 10.00 h) with DW (vehicle) or fruit extract for eight consecutive days in the fo lowing manner: Group 1 ($n = 6$), DW (1 ml/100 g/day Group 2 ($n = 6$) extract (1 ml/100 g/day), and Group ($n = 6$), extract (2 ml/100 g/day).

Another group of six, day 7 pregnant rats was divided int three groups ($n = 2$) and given vitamin A (US Vitemin Lt Bombai, India) in olive oil (15,000 U/kg) intramuscularly o days 8, 9 or 10 of pregnancy. This group served as a positiv control.

On day 20 of pregnancy all treated rats were anaesthetize using ether (BDH Chemicals, Poole, UK). The peritone cavity and uteri were opened and examined *in situ* for th