13. EMBRYOTOXIC EFFECT OF *PLUMERIA RUBRA*

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Many plants are well known for their medicinal properties, and traditional medical practice based on plants, forms a substantial part of the health care system in many developing countries. *Plumeria rubra*, a native of Mexico is a deciduous tree with an abundance of sticky, milky latex. Ethnomedical reports indicate that it has been used as a febrifuge, a purgative, and in the treatment of leprosy. It is also reported to have hypoglycaemic properties. However, the most widely reported usage of this plant appears to be an account of its activity on reproduction. The fruit, latex and other unspecified parts of the plants have been administered orally as abortifacients, while branches are reported to have been used intra-vaginally to produce abortion.

Despite the Ethnomedical information available, studies on biological tests are limited. In this study, a bioassay using pregnant rats was used to verify Ethnomedical claims that *Plumeria rubra* is an abortifacient. The stem bark of *Plumeria rubra* collected from locations around Peradeniya was separately and exhaustively extracted with hot water and 95% ethanol, using soxhlet. Subsequently the stem bark was sequentially extracted with petroleum ether (PE), dichloromethane (DE) and methanol (ME). Proven fertile males and virgin female Sprague-Dawley rats were used for the bioassay. Females weighing 180 - 200g were individually housed and their vaginal smears examined daily to determine cyclicity. The females showing regular cycles were mated and the day on which sperms were present in the vaginal smear was designated day-1 of pregnancy. Each extract suspended in polyvinyl pyrrolidone (PVP) was administered orally to pregnant rats from day 1 to day 10 of pregnancy. The dose was determined daily according to body weight (g/kg). A treatment group consisted of 10 rats, and a control group of 10 rats received PVP only. All animals were autopsied on day 16 of pregnancy, and the number of pregnant animals in the treated and control groups was noted. Additionally, the number of implantation sites, normal foetuses and corpora lutea were counted. The results were subjected to statistical analysis.

In conformity with the usual Ethnomedical practices, the preliminary studies were carried out with the hot aqueous extract and it was found to be toxic at a dose of 3.1 g/kg. Also, no antifertility activity was detected. A dose of 2.0 g/kg showed equivocal antifertility activity and this prompted studies using other solvents. The hot ethanol extract was found to be significantly active although toxic at a dose of 1.5 g/kg. A lower dose of 0.75 g/kg also showed significant activity and only six of the ten animals were pregnant. In the control group all animals were pregnant and the difference was significant. The PE extract when administered orally at a dose 1 g/kg did not show any activity. The DE and ME extract at doses of 1.3 and 1.5 g/kg respectively showed marked effects on pregnancy. At autopsy only one rat from the DE treated group was pregnant while five animals were pregnant in the ME treated group. All animals were pregnant in the control and PE treated groups. The reduction in the number of pregnant rats in the DE and ME treated groups was statistically significant. The results obtained with the DE and ME extracts were reproducible in repeat assays.

An off-white solid isolated from the DE extract contained the compound plumieride as the major constituent with some impurities. This compound which is an irridoid glycoside also showed significant activity. Six of the ten treated animals showed implantation sites, but only four of these showed normal foetuses. It was possible to identify a pure compound fulvoplumerin from the PE extract. This compound like the parent extract, was devoid of any activity on reproduction in the rat.

Toxic symptoms observed in these experiments included reduced food intake, loss of body weight and diarrhoea. Two deaths were recorded in the DE treated group. The weight loss observed with some extracts which showed significant anti-fertility activity, varied from slight to moderate to large. It was also observed that treated animals gained weight after dosing was stopped indicating that the toxic effects are reversible.

Overall, the results indicate that the stem bark of *Plumeria rubra* is Embryotoxic causing foetal death and subsequent resorption. Further work should be carried out on *Plumeria rubra* to determine whether active constituents could be separated from the toxic constituents. In addition, investigations on plumieride are merited in order to determine its role in fertility regulation, and it is essential that an authentic sample of plumieride is tested for anti-fertility activity.

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