Evaluation of reproductive performance and their repair in diabetic female swisss albino mice through *Carica papaya* leaf

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Abstract: The experiments were performed on female swiss albino mice, reproductive performance observation in alloxan monohydrate induced diabetic mice treated with aqueous leaf extract *Carica papaya* for 56 days (8 weeks) in three groups. Simultaneously the results of control (Group 1) and diabetic mice (Group 2) were compared to establish the sequential changes in reproductive performance in them. A sharp decrease was noticed in litters count in alloxan monohydrate induced diabetic mice from 11.92 ± 0.85 to 4.00 ± 0.34. In diabetic mice, it was increased to 8.90 ± 0.56 when mice were fed to aqueous leaf extract of *Carica papaya* at one time at a fixed dose of 150 mg/kg body wt per orally administration. The total dose of monohydrate ($450mgkg^{-1}$ bw^{-1}) was administered in three injections at interval of 48 hrs ($150mgkg^{-1}bw^{-1}$) each time.

Index Terms – Alloxan monohydrate, *Carica papaya* leaf, Aqueous extract, Scanning electron microscope

1. INTRODUCTION

Diabetes is a serious metabolic syndrome and also considered as a leading cause of mortality in the world. It is caused by the deficiency or inadequate production of insulin by pancreas that result in increase or decrease in concentration of glucose in the peripheral blood (RajGopal *et. al.*, 2008).

The treatment for diabetes consists of the administration of either insulin or other hypoglycemic agents in conjunction with recommendations for dietary control and physical exercise. However, these hypoglycemic agents can cause adverse effects such as Hypoglycaemia, Gastrointestinal disorders, rend toxicity and hypotoxicity (Sudasinghe and Peiris, 2018).

Diabetes brings various associated disease which adversely affecting the human health and some time fatal if not taken care properly. According to Basu *et. al.* (2014), in 2030 diabetes became epidemic and the main threat to human life and emerges as the leading given to mortality as it caused about 10 lakh, deaths in the century (Sinha *et. al*., 2018).

So the present study was aliening with these facts and performed on the Diabetic mice which were treated with aqueous leaf extract of *Carica papaya* to see the reproductive performance remedial option for the diabetic surfers in developing countries.

2. MATERIALS & METHODS

2.1 Plant material:

Fresh leaves of *Carica papaya* were collected and shade dried from plants grown in the University Department of Botany campus, of T. M. Bhagalpur University, Bhagalpur. The dried leaves were crushed to powder with help grinder and were kept in air tight container separately until use.

2.2. Preparation of aqueous extract:

Powder of *Carica papaya* leaves (100g) were boiled in 200 ml of distilled water then filtered through using whatman's filter paper No.41. The extracted filtrate has concentration of 150mg/ml. This crude filtrate was used as treatment doses and administered orally to the experimental animals groups at the concentration of 150mg/kg body weight per day for 8 weeks (Pochapski *et.al*, 2011).

2.3. Induction of diabetes and experimental setups:

Diabetes was induced in mice by intraperitonial injection of 150mg/kg body weight of Alloxan monohydrate (5% w/v) freshly dissolved in physiological saline immediately before use (Dunn and Meletchie, 1943).

The diabetic state was confirmed after 48 hrs of Alloxan monohydrate injection. The animals which presented blood glucose level above 200 mg/dl as well as with clinical signs of polydipsia, polyuria and polyphagia were selected for the experiments (Jennigs *et.al*, 1983 and Sacs, 1997).

Experimets:

Nine sets of mice with a ratio of three females to one male were taken from each type of experimental animal that is, nine females and three males of control type (Group 1). Again nine females and three males of diabetic mice (Group 2) and nine females and three males of diabetic mice treated with aqueous leaf extract of *Carica papaya* for entire gestation period (Group 3).

In the whole experimental protocol, 27 females and nine males were taken. Sexual intercourse among control animal was observed as pregnant mice confirmed by the presence of vasinal plug, in all nine sets of experimental animal including control mice. Whereas, the decreased value was recorded among only one set of alloxan monohydrate induced diabetic mice.

The experiments were performed on mice reproductive performance observation in alloxan monohydrate induced diabetic mice treated with aqueous leaf extract of *Carica papaya* for 8 weeks (Group 3) and simultaneously compared with control (Group 1) and diabetic mice (Group 2) to establish the sequential changes in reproductive performances in them.

Evaluation of pregnancy, fertility rate %, gestation length (days), death during delivery (%), evaluation of implantation site, implantation loss, live pup at birth, dead fetus, abnormal fetus, survival rate (0 - 4 days %) and litter count of control mice (Group1), diabetic mice (Group2) and aqueous leaf extract of *Carica papaya* supplemented to diabetic female mice (Group 3) were studied. The total experimental protocol was maintained for 56 days after induction of diabetic following Zarrow *et.al.* (1964).

3. RESULT AND DISCUSSION

The breeding was found to have performed in all the three sets of mice of Group -2 but the ratio was comparatively lower. While among animals that fed with aqueous leaf extract of *Carica papaya*, the recorded breeding performance showed positive corrective value in comparison to Group - 3 mice. The percent fertility rate was recorded minimum 70.37 percent in diabetic mice and this value was increased to 81.48 % in Group - 3. While in control it was 96.29 %.

Gestation length of control mice was found to be 19.80 ± 0.58 days. Which are increased to 22.15 ± 0.52 days in Group - 2. The gestation length was found to be decreased to 20.28 ± 0.42 when mice were fed with aqueous leaf extract of *Carica papaya* in Group-3. Live pregnant at delivery was 26 in control mice. In diabetic mice, it was decreased to 17 which were increased to 22 when mice were fed to aqueous leaf extract *Carica papaya*. Death during delivery was prominent in diabetic mice which were 15.00% when compare to control which 0% while in aqueous leaf extract of Carica papaya was fed group it was 8.33% establishes the protecting effect of *Carica papaya*. Death during study was also found to be decreased from 03 to 02 when diabetic mice fed with aqueous leaf extract of *Carica papaya*.

Control animal showed 312 implantation sites which was found to be decreased to 170. In diabetic mice when mice fed with aqueous leaf extract of *Carica papaya* at fixed dose, implantation site was found to be increased to 252. Percentage implantation loss was observed maximum in diabetic control which was 57.9 % and this was reduced to 20 % in Group-3. Live pups at birth of control mice were found to be 310 which decrease to 68 in Group-2. The number was found to be increased to 196 when mice were fed to Group-3. Dead foetus was 4 in control mice. In diabetic mice, it was increased to 14 which were decreased to 10 when mice were fed to aqueous leaf extract of *Carica papaya*. Abnormal foetus was increased in diabetic mice which were 15 and 12 respectively when compared to control which was 00. Survival rate (0 - 4 days) % was also found to be increased from 66.17 to 89.28 when diabetic mice fed with aqueous leaf extract of *Carica papaya*. The control animal showed 11.92 ± 0.85 litters per mice. A sharp decrease was noticed in litters count in alloxan monohydrate induced diabetic mice from 11.92 ± 0.85 to 4.00 ± 0.34. In diabetic mice, it was increased to 8.90 ± 0.56 when mice were fed to aqueous leaf extract of *Carica papaya*. The control animal showed 12.00 ± 0.78 implantation site per animal in uterus.

Table 1.1 :- REPRODUCTIVE PERFORMANCE OF DIABETIC MICE AND THEIR REPAIR BY AQUEUOS LEAF EXTRACT OF *Carica papaya*

Parameter	Group 1	Group 2	Group 3
Pregnant per group (Reproductive performance)	26	20	24
% Fertility rate	96.29	70.37	81.48
Implantation site	312	170	252
Implantation site Per animal	12.00±0.78	8.50±0.38**	10.50±0.68*
% Implantation loss (mean percentage)	3.6	57.9	20
Gestation length (Days)(Mean + SE)	19.80±0.58	22.15±0.52**	20.28±0.42**
Live pregnant at delivery	26	17	22
% Death during delivery	0	15.00	8.33
Death during study	0	3	2
Live pups at birth	310	68	196
Dead foetus	4	14	10
Abnormal foetus	0	15	12
% Abnormalities of foetus	0.00	20.80	5.02
Survival rate (0 - 4 days)	300	45	175
% Survival rate (0 – 4 days)	91.07	66.17	89.28
Litter count (Number ± S.E)	11.92±0.85	4.00±0.34**	8.90±0.56**
% Survival of litter count	96.77±2.52	80.52±2.25**	91.10±8.21**

(Group 1- Control; Group 2- Diabetic; Group 3- Diabetic+ *Carica papaya*); N= (Female- 27 and Male- 9), Values are expressed as mean ± SEM Values are statistically*significant ($p<0.05$);**highly significant ($p<0.01$)

In diabetic mice, there was a progressive reduction in the implantation site number per uterus per animal. The number of implanted embryo was recorded to 8.50 ± 0.38 in Group-2 and 10.50 ± 0.68 in Group-3 respectively. Diabetic mice when fed with aqueous leaf extract showed insignificant change in implantation site (Table 1.1).

Reports on phytochemical analysis of *Carica papaya* leaves revealed that they are rich source of alkaloids, glycosides, minerals, vitamins and many others compounds (Juarez-Rajop *et.al*, 2012) which is good for health. The reproduction process in the mammalians required various nutritional and vitamins which improves the fertility, fetus condition and especially its antioxidant property. The reproductive performance improvement through *Carica papaya* extract may also be, because of its other properties like anti inflammatory property which may prevent inflammatory damage to the mother and fetus, immuno modulatory property and antioxidant property (Alarcon-Aguilara *et.al*, 1998). Thereby reducing the oxidative stress mechanism seems to be important in *Carica papaya* leaves (Indran *et.al*, 2015) which may be improving reproducibility.

4. CONCLUSION:

The aim of the present study was to investigate the adverse effect of alloxan monohydrate induced diabetes can harm on reproductive abilities of female albino mice. The result obtained in reproductive physiological observation showed that alloxan monohydrate induced diabetic mice with control female mice had adverse effect on female reproductive system and fertility due to elevation in blood glucose level (Azuma *et. al.*, 2006).

The number of implantation site was significantly reduced which was further ameliorated by *Carica papaya* leaf extract

supplementation (Table 1.1).

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