

# Effects of Date Extract on Paracetamol Induce Nephrotoxicity in Rabbits

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## ABSTRACT

**Aim:** To examine the effect of date extract on paracetamol provoke nephrotoxicity in Rabbits.

30 Rabbits were selected for this study;

**Methods:** Rabbits were selected by random sampling for five stratum six rabbits in each stratum. They were kept under treatment for 14 days, The first stratum was control stratum no treatment given to rabbits. The second stratum was diseased stratum paracetamol given to rabbits of with pattern 2g/kg/day.

**Results:** The rabbits of third stratum were treated date extract 400g/kg/day seven days before paracetamol administration. The rabbits of fourth stratum were treated with paracetamol 2g/kg/day seven days before date extract administration. The rabbits of fifth stratum were treated 2g/kg/day along with date extract 400g/kg/day. The remarkable increase observed in serum urea and serum creatinine concentration in rabbits exposed nephrotoxic dose of paracetamol. The date extract treated rabbits show improvement in increased BUN and SC,

**Conclusion:** The exposed rabbits were then treated with date extract and this led to improvement in recovery from the toxic insult. The date extract, in addition to this, also helped in preventing the nephrotoxicity.

**Keywords:** Nephrotoxic, Date Fruit Extract, Paracetamol, Rabbits

## INTRODUCTION

Valuable Allopathic and Herbal medicine are produced from Plants (Abdelrahman, 2012; Iwu, 2014). The most Drugs and Toxins copper, arsenic, cadmium, and natural occurring toxins as mycotoxins, pyrrolizidine alkaloids, and bacterial toxins major cause of kidney failures which results Nephrotoxicity. Patients exposed to these Toxics either accidental, suicidal, environmental or due to nature of job. The kidney damage caused by the nephrotoxics could be treated with Nephro-protective compounds. Fruits and herbal extracts are studied as Nephro-protective in against drugs and chemicals in rabbits having kidney disorders. Dates contains minerals carbohydrate and vitamins which makes its quick energy source for body (A.B.M. Sharif Hossain, 2015). Date extracts also studied for cancer and infection prevention (Dagfinn Aune2018.)

The study is conducted on hypothesis that date extract can be used for prevention of drug toxicity in kidney caused by paracetamol induced toxicity rabbits.

## MATERIALS AND METHODS

Working solution of date extract prepared by using dates available in market (*Phoenix dactylifera L*). The dates were washed after removing the seeds they were kept in incubator at 50C temperature to dry the water than grinded as powder and mixed with distilled water with the ratio of 6g/1000ml with the help of electric stirrer for 48 hours at room temperature.

**Experimental protocol:** 30 Male Rabbits of weight 2kg±4g were selected for research. Rabbits were acclimatized in animal house for one week at controlled temperature and diet before they study period. Rabbits were divided in to 5 stratum each stratum contains 6 rabbits They were kept under treatment for 14 days after one week of acclimatization period, The first stratum was control stratum no treatment given to rabbits. The second stratum were diseased stratum oral paracetamol given to rabbits with pattern 2g/kg/day. The rabbits of third stratum (preventive stratum) were treated date extract 400g/kg/day seven days before paracetamol

administration. The rabbits of fourth stratum were treated with paracetamol 2g/kg/day seven days before date extract administration. The rabbits of fifth stratum were treated 2g/kg/day paracetamol along with date extract 400g/kg/day.

After study period of two weeks 15 hours fasting blood sample was draw from retro-orbital sinus through sample collection tubes. The serum collected after centrifuge blood sample at 3500RPM for 15min at 25C temperature than preserved at -4C temperature for estimation of serum urea and creatinine along with sodium, potassium and chloride.

**Biochemical analysis:** The Randox laboratory reagent was used for estimation of urea by Bertholet's Method The V-500VIS spectrometer was used for urea estimation using wavelength of 550nm. The Randox laboratory reagent was used for estimation of creatinine by Jaffe method The V-500VIS spectrometer was used for creatinine estimation using wavelength of 530nm. The flame photometer was used for the estimation of sodium and potassium.

Bivariate statistics Data analysis was done (ANOVA) for two stratum comparison study with ± standard deviation (SD) and significance level  $P < 0.05$  on SPSS 22.0

## RESULTS

In control (stratum I) there were remarkable raise ( $p < 0.05$ ) in the concentration of BUN, SC, potassium and sodium as compared with paracetamol control (stratum II) as in Table 1. On the other hand, there was no remarkable raise ( $p > 0.05$ ) in the concentration of chloride, bicarbonate of control and control stratum II. No remarkable variation ( $p > 0.05$ ) in all the functions of kidney variables between (Stratum II) and (Stratum III). There was Remarkable reduce ( $P < 0.05$ ) in SC and BUN of the Stratum II along with the Stratum IV. On the other hand no remarkable difference in other constraint. There was remarkable reduce ( $p < 0.05$ ) in the concentration of BUN, SC, Sodium, Bicarbonates and Potassium of the Stratum II and the Stratum V.

Table 1: Values are expressed as mean  $\pm$  SD using one way ANOVA. P value < 0.05 denotes significant differences between means.

Stratum	Creatinine	Urea	Sodium	Potassium	Chloride	Bicarbonate
1	1.06 $\pm$ 0.15	31.5 $\pm$ 3.00	137 $\pm$ 5.13	5.70 $\pm$ 0.50	100.34 $\pm$ 2.39	18.16 $\pm$ 0.97
2	1.34 $\pm$ 0.25	36.9 $\pm$ 4.99	189.87 $\pm$ 2.77	7.88 $\pm$ 0.44	102.67 $\pm$ 1.63	19.17 $\pm$ 0.98
3	1.13 $\pm$ 0.10	36.83 $\pm$ 5.32	140.83 $\pm$ 1.83	6.53 $\pm$ 0.41	104.88 $\pm$ 2.39	18.00 $\pm$ 1.50
4	0.90 $\pm$ 0.16	30.8 $\pm$ 2.20	15.2 $\pm$ 1.70	6.54 $\pm$ 0.96	102.1 $\pm$ 2.55	19.0 $\pm$ 1.74
5	1.05 $\pm$ 0.13	35.67 $\pm$ 5.05	135.67 $\pm$ 4.19	5.40 $\pm$ 0.87	102.0 $\pm$ 2.63	20.44 $\pm$ 0.62
P value	< 0.05	< 0.05	< 0.05	< 0.05	> 0.05	> 0.05

## DISCUSSION

Paracetamol dose is commonly coupled with several metabolic disturbances together with change in blood chemistry especially blood urea serum electrolytes along with creatinine concentration disturbance (Palani, 2009) (Ghosh, 2010). It is discovered that, ingestion of Rabbits with a toxicity of Paracetamol will cause alteration in the above mentioned biomarkers. These disturbances are, because of altered mitochondrial functioning due to paracetamol-induced death.

In this study, ingestion of the high doses of paracetamol to Rabbits developed in high levels of blood serum electrolytes, creatinine and urea levels in paracetamol toxic cluster (group II) compare to the traditional management group. These studies are in accordance with Isik. (2006), UN agency observed toxically high degree increase in BUN and SC in rabbits as of 2g/kg b.w. of paracetamol ingestion. Karadeniz. (2008) and Ajami. (2010) revealed the concentration of above mentioned biomarkers. The study demonstrates a relationship between nephrotoxicity & oxidative stress. The high level of H<sub>2</sub>O<sub>2</sub> and O<sub>2</sub><sup>-</sup> formation impart changes in the filtration process and result modification in the filtration coefficient. All these factors might decrease the capillary filtration resulting in accumulation of biochemical markers i.e., blood urea and creatinine. There was marked elevation in the concentration of electrolytes in the blood i.e., sodium and potassium in paracetamol management cluster (stratum II) compared with traditional group (stratum I). This is in accordance with the work of Yakubu (2006), UN agency reported exaggerated concentration of Sodium and Potassium in the blood of rat treated with artesunate. It's recommended that, exaggerated blood serum Na<sup>+</sup> concentration is a sign of alteration in the production of mineralocorticoid, which leads to increase the serum level of Na<sup>+</sup> or decrease production of either Pitrassin or tubular sensitivity to the hormone<sup>4</sup>.

Potassium particularly has a very significant plays role in the transmission of nerve impulses on the nerve cells to receptor cells. The increased serum potassium levels discovered in unhealthy management animals reveals an adverse impact on the pump that maintains the physiological levels of K<sup>+</sup> in living things. Hydrogen, carbonate and chloride particle showed no important changes altogether the parameters calculable. This finding was not in line with (Yakubu,2006).

This may cause to distinction in length of experiment and drug dose used. During this study, the preventive treatment of Rabbits with binary compound p. dactylifera extract revealed a big decrease on the paracetamol evoked urinary organ toxicity.

## CONCLUSION

We used a model of nephrotoxicity in rabbits associated with the use of paracetamol. The exposed rabbits were then treated with date extract and this led to improvement in recovery from the toxic insult. The date extract, in addition to this, also helped in preventing the nephrotoxicity. So we can imply that date fruit extract has renoprotective effects in face of a drug toxicity scenario.

**Conflict of interests:** Nil

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