



MITIGATION OF PARACETAMOL INDUCED GENOTOXICITY BY CURRY LEAVES (MURRAYA KOENIGII) EXTRACT IN BONE BARROW CELLS OF SWISS ALBINO MICE MUS MUSCULUS

Genetics

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ABSTRACT

Paracetamol as common analgesics as well as antipyretic drug have become one of the favourite part of human lives several reports indicates its toxicity on various organs including liver, kidney, heart with this due to production of its toxic metabolite, it causes production of free radicals which in turn damages the chromosome. In present study toxicity of chromosome was evaluated in mitotic metaphase chromosome of swiss albino mice, isolated from bone marrow cells. Structural and mitotic disruptive changes were reported and its mitigation was done by antioxidant rich curry leaves extracts. It was reported that frequency of Paracetamol treated group was significantly higher (30.66%) than that of control 4.33%, curry leaves treated group shows (3.33%) abnormalities whereas concurrent dose of both Paracetamol and curry leaves extract were 11.33%. The curry leaves shows the ameliorating effect against Paracetamol induced genotoxicity.

KEYWORDS

Paracetamol, Analgesics, Mitosis, Structural Changes, Chromosomes

INTRODUCTION:

Increasing consumption of analgesics like paracetamol has become the part of human lives, in order to get the immediate relief from minor illness. Paracetamol is an analgesics as well as antipyretic drug. available in every medical stores as OTC drug. Since It is considered as a safe drug but its overdose produce hepatic necrosis, renal failure, due to increase in lipid peroxide levels and depletion of glutathione (Abraham 2005) and also results in pulmonary toxicity (Jones & Prescott, 1997), few reports are available about genotoxic effect genotoxic effect of paracetamol (ying & yi, 2000, 2020) and its amelioration (Salah et. al, 2012, Verma and Kumari, 2020). To combat toxicity of drugs and chemicals various records shows that antioxidant rich herbs, fruits as well as vegetables play an important role one of the important medicinal cum herbal spice "Murraya koenigii" or curry leaves is favourite in every Indian houses due to its aromatic flavor beside its tasty flavour. It is recognized to be the good source of carbazole alkaloids (nafiah & Ahmad, 2014). Its antioxidant property is attributed due to presence of mahanimbine, murrayanol and mahanine (Tachibana et. al, 2003, Ningappa et al., 2005), keeping in point its antioxidant richness property the present work is designed to investigate mitigating effect of curry leaves against paracetamol induced genotoxicity in mitotic cell mice metaphase chromosome of bone marrow cells in mice.

MATERIALS AND METHOD:

A 4-6 week old swiss albino mice with an average body wt. of 25 gm. was used as test animal. Animals were caged in group and was provided proper and normal laboratory as well as nutritional condition during experimental period paracetamol tablet (500mg) was used as chemical toxicant in powdered form. Shed dried and finally powdered curry leaves was used as mitigating agent. Mice were divided into 4 experimental groups, 6 mice in each group as shown in Table – I and was subjected for the treatment for 15 days.

Table - I

Sl No.	Experiment Group	Symbol	Dose
I	Control	C	No Treatment
II	Paracetamol	P	7.10mg / kg
III	Murraya koenigii	M	100mg / kg (Deshmukh.et.al,2012)
IV	Paracetamol + Murraya koenigii	P + M	As I & II

After completion of treatment, animals were sacrificed by cervical dislocation and the slides were prepared from isolating bone marrow cells of mice followed by colchicines hypotonic acetoalcohol flame drying giemsa staining techniques by preston et. al., 1987.

300 well spread plates of mitotic metaphase chromosomes was screened under the microscope two types of abnormalities structural and mitosis disruptive changes was assessed in 4 experimental

variants. For statistical analysis student t-test was applied to evaluate the level of significance.

The findings in all 4 experimental groups shows the structural as well as mitosis disruptive abnormalities as described in Table - II.

Table - II

Treatment	Structural changes		Mitosis Disruptive		Total abnormalities	
	No.	% $\pm$ S.E.	No.	% $\pm$ S.E.	No.	% $\pm$ S.E.
C	10	3.33 $\pm$ 1.03	3	1.00 $\pm$ 0.57	3	04.33 $\pm$ 1.17
P	68	22.06 $\pm$ 2.41 ^a	24	8.00 $\pm$ 1.56 ^a	92	30.66 $\pm$ 2.66 ^a
M	6	2.00 $\pm$ 0.8 ^b	4	1.33 $\pm$ 0.66 ^b	10	03.33 $\pm$ 1.03 ^b
P+M	26	8.66 $\pm$ 1.62 ^{bc}	18	6.00 $\pm$ 1.37 ^{ab}	34	11.33 $\pm$ 1.82 ^{abc}

Incidence of chromosomal abnormalities in mitotic cell of mice treated with paracetamol at Murraya koenigii leaves.

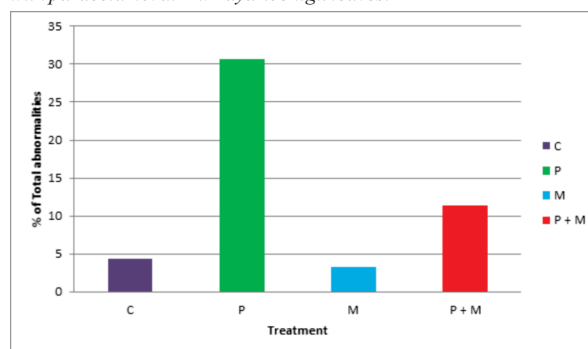


Fig.1:- Graph Showing Total Abnormalities In Mitotic Chromosome Treated With Paracetamol, Curry Leaves And Concurrent Treatment Of Both In Four Different Group Of Mice.

RESULTS:

All the 4 groups treated with paracetamol have shown both structural as well as mitosis disruptive abnormalities.

The Frequency of Paracetamol treated group was significantly higher (30.66%) than that of control 4.33% structural abnormalities reported in paracetamol treated group was 22.06% and mitosis disruptive changes were 8%.

Both values were significantly higher than control structural abnormalities include chromatid break, Acentric fragments, Ring

Chromosome, Chromatid gap and iso-chromatid gap.

Mitosis disruptive changes included polyploidy, clumping, stickiness, pulverisation and hypoploidy (Table II) The values for curry leaf extract alone treated group were reported (3.33%) as total abnormality. It did not produce any significant change in respect to control (4.33%). Both structural (2%) and mitosis disruptive changes were (1.33%) in curry leaves treated group remained insignificant in comparison to control.

In animals treated with concurrent dose of paracetamol and curry leaf extract, the structural abnormality was (8.66%), Mitosis disruptive changes were (6.0%) and total abnormalities were 11.33%. In the respective group the occurrence of structural mitosis disruptive changes and total abnormalities were significantly less than paracetamol treated group.

Among the structural group of abnormalities chromatid breaks, rings, acentric fragments were decreased and in mitosis disruptive changes polyploidy were decreased.

The results thus indicates that paracetamol is a potent genotoxic agent and concurrent dose of paracetamol with curry leave extract was effective in minimizing the paracetamol induced genotoxicity in terms of structural changes as well as mitotic disruption changes.

DISCUSSION:

The results suggest that paracetamol induces genotoxicity at structural level as well as causes mitosis disruptive changes. This may be due to the formation of toxic metabolite of Paracetamol, NAPQI which inhibits the mitochondrial. ETS chain functioning, thus results into the production of reactive oxygen species. (Jaeshka et. al 2012) or free radicals. This ROS damages have the potential of interact with cellular ingredients containing deoxyribosyl backbone of DNA or DNA bases the other possible mechanism for causing genotoxicity may be inhibition of ribonucleotide reductase and increase in cytosolic or intracellular calcium level. On the other hand the mitigating property of curry leaves may be attributed due to presence of bunches of antioxidants, vitamins flavonoids, terpenoids and carbozol aldoids which work as free radical scavengers and thus successfully ameliorate the genotoxicity induced by paracetamol.

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