# THE EFFECTS OF THE LOW DOSE BROMINATED FLAME RETARDANT BDE 209 ON RENAL FUNCTION IN *WISTAR* RATS

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**STUDY**

Widely used flame retardant, decabrominated diphenyl ether (BDE-209), is known for its effects on the liver, endocrine and neurological effects. However, it is not extensively tested for the effects on the kidney. In this study, we evaluated its effect on renal function after subacute exposure.

Healthy young adult male albino *Wistar* rats weighting 200–250 g at the beginning of experiment were housed in cages in climate-controlled facility. The constant photo-period (12 h light:12 h dark) and unlimited food and drinking water supply were provided throughout the study. The experiment has been conducted in accordance with Guidelines for animal studies issued by Ethics committee of Military Medial Academy in Belgrade, Serbia.
Animals had been accommodated to the laboratory conditions for one week before they were randomly assigned into control and treatment groups, of seven animals each. The rats were treated by oral gavage for 28 days in a volume of 1 mL/kg b.w. of BDE-209 suspension. Five treated groups were receiving BDE-209 in the form of suspension in dimethyl sulfoxide (DMSO) at the dose levels of 31.25, 62.5, 125, 250 and 500 mg BDE-209/kg b.w./day. Rats in the vehicle control groups received DMSO only. Body weights were recorded and dosing volumes adjusted daily. All efforts were made to minimise suffering, and the number of animals used was kept at minimum by experimental design. During the experiment, rats' body weights, clinical signs of poisoning, behavioural changes, and food and water intake, were continuously monitored. On the 28th day, rats were weighted and sacrificed by decapitation. The blood samples were taken on that occasion.

Animals' serum samples were examined by spectrophotometric method on Roche Cobas 6000 to determine creatinine and urea concentrations. For urea, test with ureasa and GLDH was used. For creatinine, Jaffe reaction without deproteinisation was used.

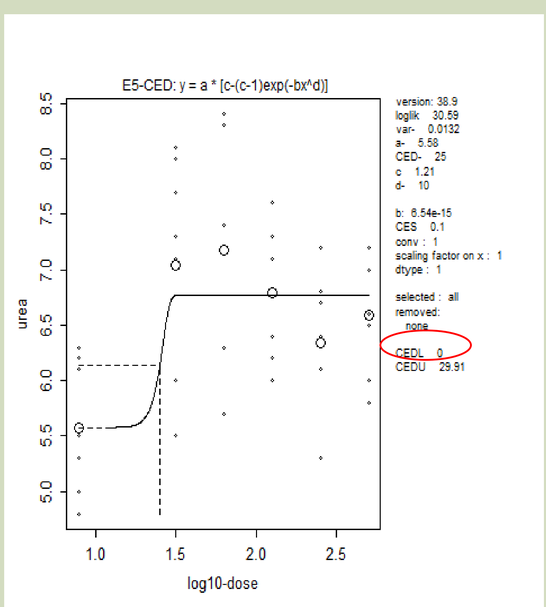
In order to apply Benchmark dose (BMD) approach for the dose-response modeling, the data on urea and creatinine levels in serum of rats treated with BDE-209 were analysed by PROAST software package developed by the Dutch National Institute for Public Health and the Environment. This approach allows the dose-response data to be statistically evaluated, by fitting a dose–response model to the data. Fitted models were selected from the nested family of models, including model 5: y= a(c-(c-1)) exp(b xd) assigned in figures as E5. In the models, the parameter *a* represents the background response, *b* reflects the "slope" or the "strength" of the response, *c* is maximal response relative to the background level, and d is steepness (Slob, 2002). Benchmark dose is the dose level responsible for low but measurable change in response (benchmark response, BMR). The terms critical effect size (CES) and critical effect dose (CED) are used instead of BMR and BMD when obtained data are continuous, as in this study (Slob, 2002). In this study, the software was used for deriving CED05 from the fitted model for observed effects on serum urea and creatinine. To take into account statistical errors in data sets, the confidence interval around the CED is also calculated.

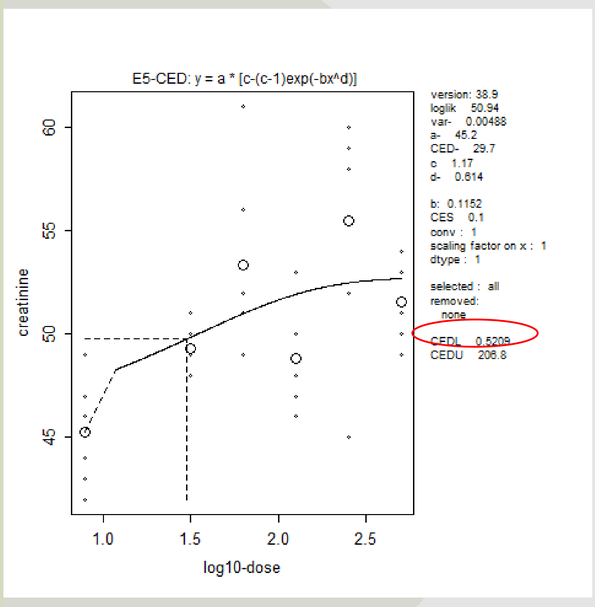
**RESULTS**

A dose-response relationship for chemical treatments in the case of both creatinine and urea serum levels has been confirmed using PROAST software. Associated Benchmark doses (BMDs) of 10% and its lower confidence limits (BMDLs) derived from the fitted models were:

29.7 and **0.52** mg BDE-209 /kg bw for creatinine, and

25 and **0** mg BDE-209 /kg bw for urea.




| Group | Mean urea (mmol/L) | Mean creatinine (µmol/L) |
|---|---|---|
| DMSO | 5.60 ± 0.61 | 45.29 ± 2.43 |
| mg BDE-209 /kg bw / day | | |
| 31.25 | 7.10 ± 1.00 | 49.29 ± 0.95 |
| 62.5 | 7.25 ± 1.07 | 53.50 ± 4.32 |
| 125 | 6.81 ± 0.61 | 48.86 ± 2.34 |
| 250 | 6.37 ± 0.62 | 55.71 ± 5.38 |
| 500 | 6.61 ± 0.56 | 51.57 ± 1.81 |

**CONCLUSION**

**The BMD/BMDL ratios above 10 indicate more information is needed to derive a health-based guidance value. Results indicate that BDE-209 may affect kidney filtering capacity.**

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