Inferences from targeting *CYP450* modulation to decrease the risk of induced cataract in the experimental model?

Dear Editor,

This refers to a well drafted article by Patel *et al*., published in a recent issue of *Indian Journal of Ophthalmology*.[1] The present study is based on the hypothesis that basic pathology for cataract is conversion of excess glucose to sorbitol (which can cause cataract) by enzyme aldose reductase using NADPH as a cofactor, and electron transfer from NADPH that depends on the cytochrome P450 system (CYP450). It was postulated that by inducing or inhibiting cytochrome, one can alter the activity of aldose reductase, formation of sorbitol, and hence modulate the occurrence of cataract. The authors have made attempts to prove this by using pioglitazone as CYP450 inducer and nifedipine as CYP450 inhibitor, and used statistical tests to establish the significance.

We would like to draw the attention of the authors on the below-mentioned points:

1. Use of galactose in the present study in diet fed to the rats for accelerating the process of cataract. In a similar experimental study on rats by Tomlinson, he had opined that rats fed on galactose are not a good model of diabetes and the subsequent induction of cataract. More so, galactose fed animal models lead to a subsequent clinical failure of aldose reductase inhibitors.[2]
2. Role of pioglitazone in cytochrome modulation is questionable but there are evidences that it has a weak inducer effect on CYP450 inducer; hence, the use of pioglitazone in the present study has made the inferences of the present study doubtful.[3-5]
3. Nifedipine was used as an inhibitor in the present study. Liver is the major site for nifedipine metabolism.[6] In addition, as hypothesized that P-glycoprotein (P-gp) is responsible for the large inter-individual difference in CYP3A-mediated drug disposition is not true with nifedipine because it is not a substrate of P-gp.[7] Therefore, nifedipine pharmacokinetics must be crucially determined by total liver CYP3A activities, as nifedipine does not directly modulate the activity of aldose reductase, which is absent in the liver, and where most of the nifedipine is expected to undergo first-pass metabolism.[8] Therefore, some other agent with a better CYP450 inhibitor should have been used.
4. Finally, to test the association, authors have used analysis of variance (ANOVA) and the post hoc Tukey test, whereas the entire results are expressed as the percentage of total number of lenses affected. Hence, the data set is expressed as nominal data, and thus the 'Chi-square test' could have been a better choice instead of ANOVA in the present condition.

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