Effect of Ashwagandha on pharmacokinetic parameters of phenytoin in Epileptic rats

Nagaraj B# and Veeresham C*

* University College Pharmaceutical Sciences, Kakatiya University, Warangal urban – 506001, TS, India. Email: ciddiveeresham@yahoo.co.in
# University College Pharmaceutical Sciences, Kakatiya University, Warangal urban – 506001, TS, India. Email: bnrpharmacy@gmail.com

Objective: The present study was aimed at evaluating the pharmacokinetic interaction between Ashwagandha with phenytoin. In addition, it was also aimed at finding out the effect of ashwagandha on the oxidative stress induced by long term administration of phenytoin.
Introduction: Phenytoin is commonly prescribed antiepileptic drug. Studies have also revealed that anticonvulsant drugs such as phenytoin lead to increased oxidative stress in the epileptic patients. *Withania somnifera* is popularly known as Ashwagandha. *W. somnifera* is known to modulate the oxidative stress markers of the body. The root extract significantly reduced the lipid peroxidation and increased thesuperoxide dismutase (SOD) and catalase activity. In the pretext of avoiding the risks associated with oxidative stress, epileptics tend to use herbal preparations rich in antioxidants, which may lead to herb-drug interactions.
Methods: Epilepsy in rats was induced by Pentylenetetrazole kindling method. Epileptic rats were divided into 4 groups containing six rats in each, the test group (II) is treated with ashwagandha (200mg/kg) for seven days and on 8th day groups I(control) and II were administered with phenytoin (40mg/kg) serum samples were collected, estimated for phenytoin in serum using validated HPLC method. Treatment with ashwagandha was continued for 28 days for group II. Phenytoin was administered alone for group III and combination of ashwagandha and phenytoin for group IV once a day for 28 days. Total antioxidant status was estimated for all the groups at 0, 7, 14, 21, and 28 days. The pharmacokinetic parameters are calculated using Winnonlin software.
Results: From the pharmacokinetic results, about 1.16 and 1.21 folds enhancement was observed in AUCtotal and Cmax of phenytoin respcetively in test group, compared with control group but, not much significant difference was noticed in other parameters.The ashwagandha showed favourable effect on bioavailability of phenytoin which may not be significant at clinical level. The effect of the combination of ashwagandha with phenytoin in group IV found gradually increased ($p < 0.01$) in total antioxidant status when compared with group III, and with epileptic control (group I) at all time intervals of the study.
Conclusion: Therefore, the results suggestive that, the Ashwagandha might be advantageous as an adjuvant to phenytoin therapy in epileptics as an anti-oxidant in an appropriate quantity. However further studies are required to confirm this in epileptic patients.

Keywords: Ashwagnadha, Phenytoin, Epileptic rats, Pharmacokinetics.

References: Bhattacharya SK, Satyan KS, Ghosal S. Antioxidant activity of glycowithanolides from Withania somnifera. *Indian J Exp Biol.* 1997; 35: 297-9.

Dhuley JN, Effect of ashwaghanda on lipid peroxidation in stress induced animals. *J Ethnopharmacol* 1998; 60: 173-8.

Harish Chandra R and Veeresham C. Herb – drug interaction of noni juice and Ginkgo biloba with phenytoin. *Pharmacognosy Journal*. 2011; 2(18): 33-41.