OMICS Group Conferences
Accelerating Scientific Discovery
2nd International Summit on Toxicology
October 7-9, 2013 Hampton Inn Tropicana, Las Vegas, USA

Factors affecting reproducibility of proteasomal inhibition following PSI systemic administration to experimental animals

Salma Bukhatwa

Benghazi University, Libya

Abstract

Repeated systemic administration of proteasome inhibitor I (PSI, [Z-Ile-Glu(O*t*Bu)-Ala-Leu-CHO], Calbiochem, Lutterworth, UK) to rats causes progressive motor deficits and nigral dopaminergic cell loss. There is a major controversy over the reproducibility of these findings. Many factors including dose, route of administration, time of the day observation is recorded, species variability and strain susceptibility have been all reported to affect systemic actions of PSI. However, reasons for lack of reproducibility of effects of PSI between laboratories require further investigation. According to manufacturer instructions, sterile dimethylsulphoxide (DMSO) or ethanol can be used as solvents for PSI. Both DMSO and ethanol are irritants and cause skin problem which is a limitation of their systemic use in experimental animals. No other solvent for PSI has been identified up till now. In this study, PSI (8mg/kg) dissolved in alternative solvent [10%DMSO/polyethylene glycol (PEG)] was administered subcutaneously to female Wistar rats on 6 occasions on alternative days over 2 weeks. Rats were assessed for motor function on a weekly basis up to 5 months after the end of PSI treatment. Decreased locomotor activity and neuronal loss in substantia nigra were observed following administration of PSI dissolved in ethanol but not 10%DMSO/PEG mixture. Then, 10%DMSO/PEG is not a suitable vehicle for PSI administration in rats. This could be due to a problem in PSI absorption from site of its application, highlighting type of PSI vehicle and other factors relate to PSI absorption as new factors to be considered in explaining the lack of reproducibility of PSI effects.

Biography

Salma Bukhatwa has completed her PhD in 2008 at King's College London, London, UK. Currently she is assistant professor doing teaching of Pharmacology and Toxicology to undergraduate Pharmacy students at Benghazi University, Benghazi, Libya. She published few articles but in reputed journals. She has participated with more than 20 abstracts in judged conferences in different parts of the world.