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Research Article

Comparison of Nanoemulsion and Aqueous Micelle Systems of Paliperidone for Intranasal Delivery

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Abstract. The objective of the study was to develop and compare the efficiency of nanoemulsion and aqueous micelle system of Paliperidone on intranasal administration. Both the formulations were evaluated for physical parameters such as globule size, pH, viscosity, conductivity and *in vitro* drug release studies. The reduction in spontaneous motor activity of L-dopa and Carbidopa-treated Swiss Albino mice on intranasal administration of nanoemulsion and micellar system of Paliperidone was compared with plain drug suspension. Histopathological evaluation of formulation treated nasal mucosal membrane was performed. Nasal spray device was evaluated for spray pattern and volume per actuation. Globule size of micellar system and nanoemulsion was found to be 16.14 & 38.25 nm, respectively. *In vitro* release of drug from micellar system was found to be 1.8-fold higher than nanoemulsion. The loading of drug in nanoemulsion was found to be superior (2.5 mg/mL) when compared to micellar system (0.41 mg/mL). The spray pattern of micellar system and nanoemulsion from the device was elliptical and circular, respectively. The locomotor activity of L-dopa and Carbidopa-treated Swiss albino mice was found to be 1096.5±78.49, 551.5±13.43 and 535.5±24.75 counts/min in case of plain drug suspension, micellar system and nanoemulsion, respectively. The intranasal administration of developed formulations showed significant difference ($p<0.01$) in the locomotor activity when compared to intranasal administration of plain drug. Thus it can be concluded that both the developed formulations have shown improved *in vivo* activity on intranasal administration and pose great potential for delivery of Paliperidone through intranasal route.

KEYWORDS: intranasal; micelle systems; nanoemulsion; paliperidone; spontaneous motor activity.

INTRODUCTION

Schizophrenia is a serious chronic and disabling psychotic disorder, often characterized by abnormal social behavior with failure to recognize what is real. Hallucinations and delusions are some of the behaviors observed in affected patients. Diagnosis is done based on positive, negative, and cognitive symptoms shown by the patients. Occurrence of schizophrenia could be due to a variety of factors such as recreational drug use, presence of additional conditions like major depressive disorders and anxiety disorders, presence of schizophrenia in the family, and perinatal or other childhood factors (1–3). Primarily, first-generation anti-psychotics were prescribed to treat schizophrenia which showed dose-dependent extrapyramidal symptoms and thus were replaced with second-generation anti-psychotics. Paliperidone, a second-generation anti-psychotic, is a benzisoxazole derivative, indicated for short- and long-term treatment of schizophrenia. It is practically insoluble in water and has oral bioavailability of 28%. Paliperidone is commercially available as osmotic-controlled release oral tablet (OROS®). Oral route is a commercially acceptable route for administration of drugs; however, several disadvantages to this route include first-pass metabolism, efflux due to transport proteins present in the intestine, limited entry of drugs into CNS, etc. Paliperidone, also known as 9-hydroxyrisperidone, acts by blocking dopamine (D_2) and serotonin ($5\text{-}HT_2A$) receptors and thus does not show the side effects exhibited by first-generation anti-psychotics (4,5). Gutierrez-Mecinas and co-workers have proposed that D_2 receptors are present in the olfactory nerve (6). Thus, intranasal delivery of paliperidone will increase the bioavailability of the drug at D_2 receptors in the brain, reducing the schizophrenic activity (7). Furthermore, in general, intranasal delivery provides better patient compliance due to ease of delivery and non-invasiveness. It enhances drug absorption through the mucosal membrane and eliminates first-pass metabolism (8). The present research

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