Intranasal Microemulsion of Sildenafil Citrate: In Vitro Evaluation and In Vivo Pharmacokinetic Study in Rabbits

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Abstract

The purpose of the present study was to prepare intranasal delivery system of sildenafil citrate and estimate its relative bioavailability after nasal administration in rabbits to attain rapid onset of action with good efficacy at lower doses. Sildenafil citrate saturated solubility was determined in different solvents, cosolvents, and microemulsion systems. For nasal application, sildenafil citrate was formulated in two different systems: the first was a cosolvent system (S3) of benzyl alcohol/ethanol/water/Transcutol/taurodeoxy cholate/Tween 20 (0.5:16.8:47.7:15.9:1:18.1% w/w). The second was a microemulsion system (ME6) containing Oleic acid: Labrasol/Transcutol/water (8.33:33.3:16.66:41.66% w/w). The prepared systems were characterized in relation to their clarity, particle size, viscosity, pH, and nasal ciliotoxicity. In vivo pharmacokinetic performance of the selected system ME6 (with no nasal ciliotoxicity) was evaluated in a group of six rabbits in a randomized crossover study and compared to the marketed oral tablets. The targeted solubility (>20 mg/ml) of sildenafil citrate was achieved with cosolvent systems S1, S3, and S5 and with microemulsion systems ME3–ME6. The saturated solubility of sildenafil citrate in cosolvent system S3 and microemulsion system ME6 were 22.98 ± 1.26 and 23.79 ± 1.16 mg/ml, respectively. Microemulsion formulation ME6 showed shorter tmax (0.75 h) and higher AUC(0-∞) (1,412.42 ng h/ml) compared to the oral tablets which showed tmax equals 1.25 h and AUC(0-∞) of 1,251.14 ng h/ml after administration to rabbits at dose level of 5 mg/kg. The relative bioavailability was 112.89%. In conclusion, the nasal absorption of sildenafil citrate microemulsion was found to be fast, indicating the potential of nasal delivery instead of the conventional oral administration of such drug.

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