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论文

盐酸多奈哌齐胶囊及片剂的人体生物等效性研究盐酸多奈哌齐胶囊及片剂的人体生物等效性研究

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摘要：

目的建立人血浆中盐酸多奈哌齐的HPLC-MS (quadrupole)测定方法,研究盐酸多奈哌齐在正常人体内的药代动力学行为,评价其两种制剂的生物等效性。方法人体实验采用双交叉设计,20名健康受试者交叉口服国产盐酸多奈哌齐胶囊和进口片剂,服药后0.5～192 h内间隔取血。血样加入内标(盐酸非洛普)经预处理后用HPLC-MS(quadrupole)法测定,检测离子为*m/z* 380(多奈哌齐)、*m/z* 344(内标),裂解电压为120 V。计算主要药动学参数,并以片剂为参比制剂,估算国产胶囊的相对生物利用度,判断生物等效性。结果国产及进口盐酸多奈哌齐制剂的生物半衰期分别为(63±10) h和(57±9) h,达峰时间分别为(3.3±0.4) h和(3.4±1.0) h,峰浓度分别为(8.5±0.4) μg·L^{-1}和(8.1±1.0) μg·L^{-1}。以进口制剂为对照,用AUC0-192计算的国产胶囊相对生物利用度为102%±11%。结论本实验建立的分析方法灵敏、准确、简便,统计学结果表明两种制剂生物等效。

关键词： 多奈哌齐 药代动力学 生物等效性 高效液相色谱-质谱联用

Bioequivalence of donepezil capsule and tablet in human

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Abstract:

AimTo develop an HPLC-MS assay for determination of donepezil in human plasma and to investigate the pharmacokinetics and bioequivalence of donepezil capsule in healthy volunteers. MethodsA randomized crossover design was performed in 20 healthy volunteers. In the two study periods, a single 5 mg dose of either capsule or tablet was administered to each volunteer. After spiked with the internal standard (phenoprolamine) and treated with saturated sodium bicarbonate, plasma was extracted with ethyl acetate and separated with a C^{18} reversed phase column. LC-ESIMS was used in the selected ion monitoring (SIM) mode with target ions at *m/z* 380 for donepezil and *m/z* 344 for phenoprolamine. The fragmentor voltage was 120 V. The main pharmacokinetic parameters of donepezil and the bioequivalence of its two preparations were calculated. ResultsThe main pharmacokinetic parameters $T_{1/2}$, T_{max} and C_{max} were (63±10) h, (3.3±0.4) h and (8.5±0.4) μg·L^{-1} for the capsule; (57±9) h, (3.4±1.0) h and (8.1±1.0) μg·L^{-1} for the tablet, respectively. The relative bioavailability of the donepezil capsule was 102%±11%. ConclusionThe assay was shown to be sensitive, accurate and convenient. The two preparations of donepezil were bioequivalent.

Keywords: pharmacokinetics bioequivalence HPLC-MS donepezil

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