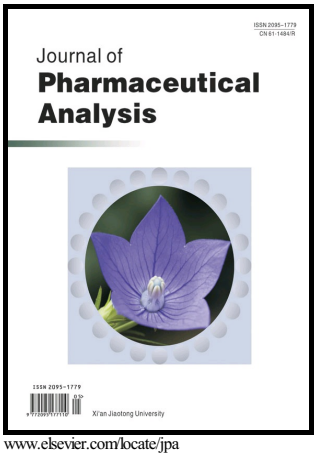

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Formulation, stability testing, and analytical characterization of melatonin-based preparation for clinical trial

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Abstract

A new institutional clinical trial assessed the improvement of sleep disorders in 40 children with autism treated by immediate release melatonin formulation in different regimens (0.5 mg, 2 mg, and 6 mg daily) for one month. The objectives of present study were to (i) prepare low dose melatonin hard capsules for pediatric use controlled by two complementary methods and (ii) carry out a stability study in order to determine an use-by-date. Validation of preparation process was claimed as ascertained by mass uniformity of hard capsules. Multicomponent analysis by attenuated total reflectance Fourier transformed infrared (ATR-FTIR) of melatonin / microcrystalline cellulose mixture allowed to identify and quantify relative content of active pharmaceutical ingredient and excipient. Absolute melatonin content analysis by high performance liquid chromatography in 0.5 mg and 6 mg melatonin capsules was 93.6% ± 4.1% and 98.7% ± 6.9% of theoretical value, respectively. Forced degradation study showed a good separation of melatonin and its degradation products. The capability of the method was 15, confirming a risk of false negative inferior to < 0.01 %. Stability test and dissolution tests were compliant over 18 months of storage with European Pharmacopoeia. Preparation of melatonin hard capsules was completed manually and stable 18 months, in spite of low doses of active ingredient. ATR-FTIR offers a real alternative to HPLC for quality control of high dose melatonin hard capsules before the release of clinical batches.

Keywords**:** Melatonin; Stability-indicating Method; High-performance liquid chromatographic; Multicomponent analysis; Clinical trial; Autism.