ICACC 2007 TUNISIA

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The Second International Congress of Applied Chronobiology and Chronomedicine

Host and Organizer

The Tunisian Association
of Chronobiology and Chronopharmacology
&
Pharmacology Laboratory
Medicine Faculty, Monastir - Tunisia

March 23-28, 2007
Tunis-Gammarth Tunisia

ABSTRACT BOOK

Volume 1

P28.

CHRONOBIOLOGICAL STUDY OF LORATADINE EFFECT ON TISSUE LIPOPEROXIDATION IN MICE

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Introduction & Objectives: Loratadine (LOR) is a specific antagonist of the H_1 receptors and an antihistaminic agent used in several allergic diseases. The present work aims at studying the effect of acute administration of LOR in mice on lipoperoxidation according to the circadian dosing-time. Lipoperoxidation was studied in three tissues (liver, kidney and brain) by measuring malondiadehyde (MDA) content, an endproduct of lipoperoxidation.

Methods: A total of 48 male Swiss Albinos mice (6 mice/dose/circadian stage) were used. All mice were aged 10 to 12 weeks and synchronized in an environmentally controlled room (temperature, 20–24°C; humidity, 45–55%) with a 12-h light/dark cycle (L/D = 12/12) for at least 3 weeks. A single oral dose of LOR (1g / kg) is administered at three circadian dosing-times (1, 9 and 17 Hours After Light Onset, HALO). Animals were sacrificed at the same circadian times of injection three days following LOR administration. The tissues were withdrawn and quickly excised and used for the determination of MDA status. Tissue proteins concentration and MDA content have been determined according to the methods of Lowry (1951) and Wasowicz & al. (1953), respectively. Data analysis were carried out by Student *t*-test and cosinor method.

Results: The 24-hour mean of MDA contents varied significantly according to both tissues and treatment. The highest and lowest values were found in renal (control: 0.21±0.02; treated: 0.16±0.01 nmol/mg prot) and brain (control: 0.03±0.002; treated: 0.05±0.002 nmol/mg prot) tissues, respectively. In the liver, LOR acute treatment increases the amplitude rhythm by 66% and shifts the acrophase toward the middle of dark span (control: 14 HALO; treated: 18.9 HALO). On the other hand, treatment with LOR induced a decrease in renal tissue of both mesor and amplitude by 24 and 28 %, respectively and a significant phase-advance of the circadian acrophase of the rhythm (11.1 HALO ± 2h *vs.* 4.7 HALO ± 1h24). Moreover, cosinor analysis revealed that acute LOR treatment delayed the circadian peak-time by 12h (control: 5.9 HALO; treated: 18 HALO) and also increased mesor and amplitude rhythm.

Conclusions: The obtained results showed that acute LOR treatment altered, after a 72h span, circadian rhythm of MDA content in liver, kidney and brain. The effects might occur through a phase shift mechanism dependent of the exposure time in the 24h scale.

Keywords: Loratadine, Malondialdehyde, Circadian rhythm, Tissue concentration, Mice