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Cardio-circulatory responses to Melatonin (MLT).

Many patients, that have received daily parenteral or oral dose of MLT, as high as 6,6 gs for 35 days (Lerner A.B. and J.J. Nordund; *J. Neural Transmission. Suppl.* 1978, **13**, 339-347) have shown no evidence of acute or delayed toxicity, even 18 years later.

MLT is scarcely directly soluble in water, so that it must be first dissolved in ethanol and then diluted with water or aqueous solutions. The effects of MLT administration can be sometimes obscured by contradictory results, owing to the purity of MLT sample, the solvent of MLT, the time of the daily cycle, the way of administration, the chronic implantation in beeswax.

5 mg MLT, taken at 06,00 pm. by a patient, one week apart, over a period of 3 months, brought about an increase of PR, RT and pulse for at least four hours after oral administration (V.T. Wynn: IV Colloquium of the European Pineal Study Group. Abstract n. 61, 1987).

In male rats, fed a complete, balanced ad libitum diet, under light schedule 12-12 (lights on at 09,00 h.), we noticed that i.p. or i.v. injection of MLT in the late afternoon caused a short but significant, although transient reduction of cardiac frequency, as well as lowering of QRS voltage. MLT as well as N-acetylserotonin have been widely recognized through the central nervous system. (Pulido O. et al.: *Neuropsychopharmacology* 1981, **5**, 573-6), and exogenous MLT can be metabolised to N-acetylserotonin (Leone R.M. e R.E. Silman: *Endocrinology* 1984, **114**, 1825-1832). The effects of pharmacological doses of MLT can probably have both a central and a peripheral source; on the other hand they could be related either to MLT or to N-acetylserotonin.

Melatonin; rat ECG; N-acetylserotonin.