

Effect of a Novel Valerian Extract on Sleep Duration, Latency, Pro-sleep Neurotransmitters and Neuronal Receptors in a Pentobarbital-Induced Sleep Model in Mice

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Objectives: Insomnia and sleep associated disorders continue to remain one of the significant health challenges affecting more than 30% of adult population. Valeriana officinalis is being used since ancient times for treatment of conditions associated with sleep. The current study aimed to validate the effect of a novel valerian (VA) extract on sleep quality and molecular mechanisms of action using pentobarbital-induced sleep model in mice.

Methods: Thirty-five male BALB/c mice were divided into 5 groups: 1) Control, 2) Pentobarbital (42 mg/kg), 3) Pentobarbital + melatonin (2 mg/kg BW) 4) Pentobarbital + VA1 (100 mg/kg BW), 5) Pentobarbital + VA2 (300 mg/kg BW). Forty-five minutes following oral treatment, mice were injected with a hypotonic dose of pentobarbital into the left side of abdomen. Sleep duration was measured as the time elapsed between reflex loss and recovery. Sleep latency was measured as the period between pentobarbital injection and sleep onset. Melatonin was

used as reference in the study. Animals were euthanized at the end of the study and analyzed for serum neurotransmitter levels and various neurotransmitter receptor levels in the brain tissues.

Results: Melatonin and VA extract increased the sleep duration and decreased the sleep latency as compared to Pentobarbital group ($P < 0.05$), wherein the VA2 group showed significantly higher improvements in sleep latency compared to VA1 and melatonin groups ($P < 0.05$). Further, both groups of valerian (VA1 & VA2) and melatonin increased the serum levels of pro-sleep neurotransmitters; serotonin, melatonin, and dopamine along with increased expression of their receptors (GABA_A R2, GABA_B R1- R2, serotonin receptor, Glutamate receptors GluA1, GluN2A, and GluN1) in the brain tissues. We also observed increased expression of modulators of apoptotic pathway and reduced oxidative stress in valerian as well as melatonin groups.

Conclusions: Valerian extract 2% powder prolongs sleep duration and decreases sleep latency in a pentobarbital-induced sleep model in mice. Further valerian extract modulated the serum levels of all three pro-sleep neurotransmitters and enhanced the expression of various sleep promoting neuronal receptors of brain involved in sleep biology in a dose-dependent manner.

Funding Sources: OmniActive Health Technologies (India) and partially by the Turkish Academy of Sciences (Turkey).