Abstract of PhD Thesis

Thesis Title: Exploring Novel Pharmacological Approaches To Attenuate Experimental Opioid Dependence Induced Withdrawal Syndrome In Mice.

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Abstract: The present study investigated the effect of SU-6656; ammonium pyrrolidine dithiocarbamate (APD); RS 102895; tributyrin; trichostatin A; N-Acetyl-Asp-Glu-Val-Asp-al; Sodium orthovanadate and SJA 7019 on propagation of morphine dependence and resultant withdrawal signs in vitro and in vivo. Morphine was administered twice daily for 5 days following which a single day 6 injection of naloxone (8 mg/kg, i.p.) precipitated opioid withdrawal syndrome in mice. Withdrawal syndrome was quantitatively assessed in terms of withdrawal severity score and the frequency of jumping, rearing, fore paw licking & circling. Naloxone induced contraction in morphine withdrawn isolated rat ileum was employed as an in vitro model. SU-6656; ammonium pyrrolidine dithiocarbamate (APD); RS 102895; tributyrin; trichostatin A; N-Acetyl-Asp-Glu-Val-Asp-al; Sodium orthovanadate or SJA 7019 dose dependently attenuated naloxone induced morphine withdrawal syndrome both in the in vivo and in vitro models. Therefore, it may be concluded that the inhibition of src-kinase; nuclear factor kappa B; chemokine CCR-2 receptor; histone deacetylase; interleukin-1-β converting enzyme; tyrosine phosphatase and calpain attenuates the development of morphine dependence as observed in the naloxone-induced precipitation of withdrawal symptoms in morphine dependent mice as well as withdrawal response in isolated rat ileum preparation.