Abstract of PhD Thesis

Thesis Title: Exploration and evaluation of novel pharmacological approaches for attenuation of nicotine dependence induced withdrawal syndrome in mice.

Candidate’s Name: Thakur Gurjeet Singh, Reg. No.: CUPB/01/Ph.D/11/20

Abstract: The present study investigated the effect of SU-6656; ammonium pyrrolidine dithiocarbamate (APD); RS 102895; Ro 32-0432 hydrochloride; and FTI-276 trifluoroacetate on propagation of nicotine dependence and resultant withdrawal signs in vivo. The experimental protocol consisted of administration of nicotine, (2.5 mg/kg, subcutaneously), four times daily for 7 days. In order to precipitate nicotine withdrawal, mice were given one injection of mecamylamine (3 mg/kg, intraperitoneally, i.p), 1 h after the last nicotine injection on the test day (day 8). Behavioral observations were made for a period of 30 min immediately after mecamylamine treatment. Withdrawal syndrome was quantitated in terms of a composite withdrawal severity score, Jumping Frequency, Hyperalgesia and withdrawal syndrome related anxiety was assessed by elevated plus maze test results. SU-6656; ammonium pyrrolidine dithiocarbamate (APD); RS 102895; Ro 32-0432 hydrochloride; and FTI-276 trifluoroacetate dose dependently attenuated mecamylamine induced experimental nicotine withdrawal syndrome in vivo models. Therefore, it may be concluded that the inhibition of Src-kinase; nuclear factor kappa B; chemokine CCR-2 receptor; G-protein couple receptor kinase-5 and Farnesyltransferase-I to which the compounds have shown affinity, will in all probability be involved in attenuation of the development of Nicotine dependence as observed in the mecamylamine-induced precipitation of withdrawal symptoms in Nicotine dependent mice.

Keywords: Nicotine dependence; withdrawal syndrome; nicotine; mecamylamine; Src-kinase; Nuclear factor kappa B; Chemokine CCR-2 receptor; G-protein couple receptor kinase-5 and Farnesyltransferase-I.