INTRODUCTION
Self-administration models enable sensitive and reliable detection of reinforcing drugs (e.g., Mead, 2014). Intravenous self-administration is commonly used for rapid drug delivery to the central nervous system (CNS) to mimic methods of drug abuse. Self-administration of a drug on a fixed ratio (FR) schedule of drug reinforcement can determine whether or not it serves as positive reinforcer. However, FR determinations provide no information about the relative reinforcing efficacy of different drugs. This question can be answered by having animals press operant levers on an escalating response requirement within test sessions to receive intravenous drug rewards in an ascending, progressive ratio (PR) testing (Heal et al., 2015).

In this investigation, we have explored the reinforcing effect of nicotine on a FR5 schedule, and in addition, its relative reinforcing efficacy was compared against various highly abused drugs with worldwide Controlled Drug status. The drugs selected were the opiates, heroin (Controlled Drug Schedule 2 [C-II]) and remifentanil (C-II), and the psychostimulant, cocaine (C-II). The drugs and their chemical structures are shown in Figure 1.

RESULTS
• All of the doses of nicotine maintained high levels of self-administration in rats on a FR-5 schedule of drug reinforcement relative to saline (non-reinforcer).
• A wide range of doses of heroin, remifentanil, and cocaine served as positive reinforcers in rats on a FR schedule of self-administration.
• The break-points of responding for the various reinforcing doses of nicotine revealed that 15 µg/kg/infusion with a break-point of 73.4 ± 14.8 lever-presses/infusion (n = 8) was the most reinforcing dose of the drug.
• The break-point for the most reinforcing dose of nicotine (15 µg/kg/infusion) was not significantly different from the most reinforcing doses of heroin or remifentanil or a highly reinforcing dose of cocaine.

CONCLUSIONS
• Heroin, remifentanil, and cocaine were robust positive reinforcers in the test, reflecting their known profiles as highly abused drugs in humans. The relative reinforcing efficacy of nicotine determined by PR testing with break-point analysis was not significantly different from heroin remifentanil or cocaine.
• Although nicotine is a legally available and a widely used recreational drug, it nevertheless had the equivalent reinforcing efficacy in this test as three C-II Controlled Drugs.