New Product Highlights

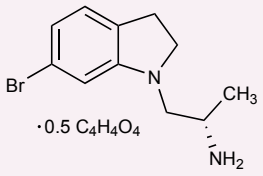
VER-3323: A novel, orally active 5-HT$_{2C/2B}$ serotonin receptor agonist that reduces food intake *Exclusively* available from Sigma-RBI

In view of the increasing prevalence of obesity in Western society, numerous pharmacological interventions are being investigated with a view to developing effective anti-obesity agents. One popular approach involves the development of selective 5-HT$_{2C}$ serotonin receptor agonists. In support of this strategy, the non-selective 5-HT$_{2C}$ serotonin receptor agonist **1-(3-chlorophenyl) piperazine** (m-CPP; Prod. No. C 5554) has been shown to lower food intake, reduce body weight and accelerate the appearance of the behavioral satiety sequence in rats [1-3], in addition to promoting decreased food intake in both normal [4] and obese human volunteers [5]. Moreover, the anorectic effect of m-CPP is absent in mutant mice lacking the 5-HT$_{2C}$ serotonin receptor [6] and is attenuated by the selective 5-HT$_{2C}$ serotonin receptor antagonist **SB-242084** (Prod. No. S 8061) in rats [7].

Recently, in an effort to develop compounds with improved 5-HT$_{2C}$ serotonin receptor selectivity and oral potency, researchers at Vernalis Group in the UK have developed a novel series of indoline alkylamine derivatives [8]. In radioligand binding studies performed on human serotonin receptors expressed in CHO-K1 cells, [^{3}H]-5-HT was used to radiolabel 5-HT$_{2B}$ and 5-HT$_{2C}$ serotonin receptors, while [^{3}H]-DOI (2,5-dimethoxy-4-iodoamphetamine) was used to label 5-HT$_{2A}$ serotonin receptors. **VER-3323** (Prod. No. V 1889) displayed high affinity for 5-HT$_{2C}$ serotonin receptors (K_i 17 nM) and 5-HT$_{2B}$ receptors (46 nM), but significantly lower affinity for 5-HT$_{2A}$ serotonin receptors (351 nM) [9]. VER 3323 bound poorly to other serotonin receptor subtypes as well as to a wide range of other neurotransmitter/neuropeptide receptors.

Of particular interest, VER-3323 (1, 3, 10 and 30 mg/kg s.c.) dose-dependently reduced food consumption in 23 hr food-deprived Lister-hooded rats over a 4 hr period, displaying a minimum effective dose (MED) of 3 mg/kg s.c. In a subsequent study, VER-3323 administered orally by gavage (10, 30 and 60 mg/kg p.o.) similarly reduced food consumption with a MED of 30 mg/kg p.o. In addition, the decrease in food intake induced by the acute administration of VER-3323 (10 mg/kg s.c.) was completely reversed by prior treatment with the selective 5-HT$_{2C}$ serotonin receptor antagonist SB-242084 [10].

These data suggest that VER-3323 is an orally active 5-HT$_{2C}$ serotonin receptor agonist that will provide a useful tool for studying the role of 5-HT$_{2C}$ serotonin receptors in food intake.



VER-3323
(Prod. No. V 1889)

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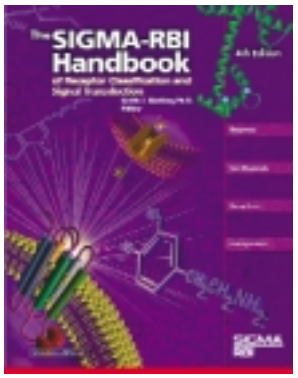

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