JL 13, An Atypical Antipsychotic:
A Preclinical Review

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ABSTRACT

The extensive pharmacological evaluation of JL 13 as an atypical antipsychotic drug has revealed a close similarity to clozapine, however with some major advantages. JL 13 was characterized as a weak D₂ antagonist, both in vitro and in vivo, with a strong affinity for the D₄ and the 5-HT₂A receptors. It has no affinity for the 5-HT₂C receptor. In vivo microdialysis experiments in rat showed that JL 13, like clozapine, preferentially increased extracellular dopamine concentrations in the prefrontal cortex compared to nucleus accumbens or striatum.

Behavioral studies showed that JL 13, like clozapine, has the profile of an atypical antipsychotic. Thus, JL 13 did not antagonize apomorphine-induced stereotypy nor did it produce catalepsy, but it antagonized apomorphine-induced climbing in rodents. It was inactive against d-amphetamine-induced stereotypy but antagonized d-amphetamine-induced hyperactivity in the mouse. Likewise, in the paw test, it was more effective in prolonging hindlimb retraction time than prolonging forelimb retraction time. Like other antipsychotic drugs, JL 13 reversed the apomorphine- and amphetamine-induced disruption of prepulse inhibition. In a complex temporal regulation schedule in the dog, JL 13 showed a high resemblance with clozapine without inducing sialorrhea, palpebral ptosis or any significant motor side effects. In rats and squirrel monkeys JL 13 induced a high degree of generalization (70%) to clozapine.

Regarding behavioral toxicology, JL 13 did not produce dystonia or Parkinsonian symptoms in haloperidol-sensitized monkeys. After acute administration, again like clozapine, JL 13 induced only a transient increase in circulating prolactin. Last but not the least, regarding a possible hematological toxicity, unlike clozapine, JL 13 did not present sensitivity to peroxidase-induced oxidation. Moreover, its electrooxidation potential was close to that of loxapine and far from that of clozapine. Taking all these preclinical data into account, it appears that JL 13 is a promising atypical antipsychotic drug.