

## ABSTRACT

### Evaluation of Olanzapine and Ziprasidone on 5-HT<sub>2C</sub> Receptors of the Isolated Rat Detrusor Muscle

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Olanzapine and ziprasidone treat symptoms of schizophrenia and psychoses. However, they have been documented to reduce bladder function in patients with antagonism of serotonin 5-HT<sub>2C</sub> receptor being implicated as the cause. This study determined the effect of olanzapine and ziprasidone on the contracted isolated detrusor muscle strip.

Detrusor muscles isolated from male Sprague Dawley rats (250-350g), were divided into longitudinal strips and suspended vertically through double ringed electrodes, connected to isometric force transducers attached to a Polyview data acquisition system. The detrusor strips were immersed in organ baths containing Krebs's solution with carbogen (95% O<sub>2</sub>:5% CO<sub>2</sub>) at 37°C. After equilibration at 0.5g, detrusor strips underwent electric field stimulation (EFS, 60 V, 0.5s duration, 10s delay, 5 Hz frequency) while adding 5-HT (0.01-30 μM and 0.1 nM-1 μM) cumulatively at half-log concentrations. Concentration response curves were obtained in the absence and presence of olanzapine (0.3 nM-3 μM) and ziprasidone (0.001 nM-1 nM) during EFS. In other experiments, 5-HT<sub>2C</sub> receptor agonist, WAY-161503 (1x10<sup>-9</sup> M to 1x10<sup>-5</sup> M) was added cumulatively at half log concentrations. Concentration response curves were obtained with WAY-161503 in the absence and presence of olanzapine (3x10<sup>-12</sup> M to 3x10<sup>-9</sup> M) and ziprasidone during EFS. Statistical analysis involved ANOVA. Significant difference in treatments was assumed with p≤0.05. Data was presented as means±SD.

The results showed that EFS induced contractions in the detrusor muscle were potentiated by 5-HT and WAY-161503. Olanzapine and ziprasidone significantly inhibited 5-HT and WAY-161503 potentiated contractions (p<0.00, p<0.00, p<0.00, p<0.014). 5-HT potentiated contractions were reduced in the presence of olanzapine (range: -41.62±53.41% to -7.41±49.87%) and ziprasidone (range: 42.04±71.40% to -9.70±62.49%). Additionally, WAY-161503 potentiated contractions were reduced in the presence of olanzapine (range:-40.90±57.48% to -81.07±113.69%) and ziprasidone (range: 3.98±172.66% to -81.17±87.50%) in a concentration dependent manner.

The results suggest that olanzapine and ziprasidone have the potential to reduce bladder contractility possibly through interaction with 5-HT<sub>2C</sub> receptors.

Keywords: Michelle Ava-Gaye Morris; olanzapine; ziprasidone; urinary retention; electric field stimulation; serotonin.