ABSTRACT: Indorenate is a central hypertensive agent, exerting its action by 5-HT1A central receptor stimulation, but also possessing a 5-HT2 peripheral receptor stimulation. Since less than 1% of the oral administered dose penetrates into the CNS, most of the compound could stimulate the 5-HT2 peripheral receptors leading to an antihyperglycemic effect. In this study we investigated which receptor subtype of the 5-HT2 family activates the indorenate to produce its antihyperglycemic effect, and we measured insulin sensitivity with hyperinsulinemic euglycemic clamp in pithed rats.

METHODS: 66 male Wistar rats were divided into groups of 6 rats. For Oral Glucose Tolerance Test (OGTT) control group (saline 1 ml/100 g po; 0.1 ml/100 g ip); (ketanserin 0.1 mg/kg ip); (L6670 1mg/kg ip); (RS-102221 1mg/kg ip); (Indorenate 5 mg/kg po). After 12-h overnight fast. Blood samples were obtained during OGTT at 0, 30, 60, 90 and 120 min, in order to measure glucose levels at each point. Another group were pithed and after used into clamp, indorenate (33.33 microg/kg/min), insulin (4 mU/kg/min) and glucose (25%, w/v, variable infusion rate).

RESULTS: Indorente has an antihyperglycemic effect In the OGTT compared to the control group and when 5-HT2c antagonist and 5-HT2B are used, it does not modify the antihyperglycemic effect of indorente, whereas ketanserin blocks the glucose decrease. On the other hand, the antihyperglycemic effect was not modified on pithed rats.

CONCLUSION: this study confirmed that indorenate has an antihyperglycemic effect on 5-HT2A, and improves insulin sensitivity.