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Antihyperglycemic effect of 5-HT₂ receptor stimulation induced by a serotonin analogue

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The role of 5-Hydroxytryptamine in the regulation of glycemia has been a controversial item for some time, however, there are recent findings suggesting that 5-HT_{1A} receptor stimulation increases the glycemia, while 5-HT₂ receptors do the opposite. Therefore, we decided to investigate the effect of indorenate, a central antihypertensive agent exerting this action by 5-HT_{1A} 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. The oral dose of glucose (2g/kg) to fasted Wistar rats was followed by a hyperglycemia that was maximal one hr later, this effect was suppressed by the previous administration of an oral dose of 10 mg/kg of indorenate, however, metformin at an oral dose of 300 mg/kg only produce a slight, but significant decrease in hyperglycemia. Pelanserine, a 5-HT₂ antagonist, blocked the effect of indorenate, but WAY 100635, a 5HT-1A agonist, did not. Indorenate also increase the glucose velocity needed to maintain blood glucose levels constant in an euglycemic insulin clamp in anesthetized Wistar rats. The present data suggest that indorenate may have a potential therapeutic usefulness in both, metabolic syndrome and in diabetic type2.

Biography

Enrique Hong chong obtained his M.D. in 1960 at UNAM and his PhD at Cinvestav in 1984, both are located in Mexico City. He worked at the Miles Institute for Experimental Therapeutics in Mexico City and then became member of the Faculty of Cinvestav, where he was the Head of the Pharmacology and Toxicology Department, and he is now Professor at the Pharmacobiology Department at Cinvestav. He has published more than 130 papers in journals with impact factor and have more than 1000 bibliographical citations to his publications.

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