

**Brain and Gastric AT1 Gene Expression  
Changes in Adult Male Albino Rats Induced by  
Chronic Immobilization Stress. The Possible  
Role of Angiotensin II Type 1 Receptor (AT1)  
Blockers**

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**BY**

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## Summary

Our study was conducted upon 60 male rats, they were divided into 6 equal groups, the first 3 groups were left wandering in their cages, the last 3 groups were subjected to chronic immobilization stress for 60 minutes every day for 10 consecutive days, 2 groups of non stressed group and 2 groups of stressed groups were given candesartan in a dose of 1 mg and 2 mg / kg.

On the tenth day Pyloric ligation were done to all groups for 4 hours then scarification were done with an over dose of anesthetic ether.

The following parameters were measured:

**A- Measurement of AT1 gene expression in brain by polymerase chain reaction (PCR).**

**B- Measurement of AT1 gene expression in pylorus by polymerase chain reaction (PCR).**

**C- Measurement of the following parameters in the collected gastric juice:**

1- Titratable acidity.

2- Pepsin activity.

3- Mucous concentration.

**D- Ulcer index in gastric mucosa.**

The results showed that stress causes marked increase in AT1 gene expression in both brain and stomach.

Also stress caused marked increase in titratable acidity, pepsin activity, gastric ulceration and decrease in mucous concentration , with use of candesartan, gene expression had decreased dramatically in both brain and stomach, also there was a significant decrease in titratable acidity, pepsin activity, gastric ulceration and increase in mucous concentration with use of candesartan.

Stress induces acute gastric mucosa lesions by a variety of mechanisms, including psychological factors influencing individual vulnerability, stimulation of specific brain pathways regulating autonomic

function, decreased blood flow to the mucosa, increase in muscular contractility, mast cell degranulation, leukocyte activation and increased free radical generation resulting in increased lipid peroxidation (*Andrade et al., 2001*)

Maintenance of gastric blood flow is important to protect the mucosa from endogenous and exogenous damaging factors, and Ang II, through AT<sub>1</sub> receptor stimulation, increases vascular tone in resistance arteries including those of the gastric vasculature leading to decreased blood flow and ischemia. ([Paul et al., 2006](#)).

With the use of candesartan, known as a potent ARB, it was clear in the results of this study that it has a great protective role regarding gastric ulceration and stress response.

The protection of gastric blood flow after administration of AT<sub>1</sub> receptor antagonists is probably mediated by inhibition of receptors localized to the endothelium of arteries located in the gastric mucosa (*Bregonzio et al., 2003*).

Lines of evidence supporting the hypothesis of a major role of brain Ang II in stress include stress-induced increases in circulating and brain Ang II levels (*Yang et al. , 1996*), high AT<sub>1</sub> receptor expression in all areas involved in the stimulation of the hypothalamic-pituitary-adrenal axis (HPA) activity, including the hypothalamic paraventricular nucleus (PVN), the median eminence (ME) and the subfornical organ (SFO) (*Tsutsumi and Saavedra 1991*).

Sustained inhibition of peripheral and brain AT<sub>1</sub> receptors by peripheral administration of the AT<sub>1</sub> receptor antagonist candesartan prevents not only the hormonal, but also the sympatho-adrenal response to immobilization stress (*Armando et al., 2001*). In addition, candesartan pretreatment prevents the activation of the brain sympathetic system during immobilization and produced anti-ulcer effect on gastric mucosa . (*Saavedra et al., 2011*).