VI Summary and conclusion:

Previous studies we constructed on Alzheimer disease concerning induction and improvement of the symptoms of the disease using several techniques and strategies.

In the present study we evaluate the possible protective effects of tempol and Telmisartan on the pathogenesis of the disease in LPS induced amyloidogenesis and neuroinflammation in mice and to achieve this goal three sets of experiment were conducted including behavioral tests, biochemical analysis and histopathological studies.

Mice were divided into five groups each group consist of about 14-18 mice. The first group was i.p injected with saline while Alzheimer's disease was induced in the other four groups through i.p injection with LPS at a dose of (0.8 mg/kg) seven days before behavioral testing one of the LPS injected groups was left untreated and the other three groups were injected with different treatments. One group was i.p injected with Tempol at a dose of (100 mg/kg) for seven days and the other two groups injected with Telmisartan in two different doses one of the at a dose of (0.5 mg/kg) and the other one at a dose of (0.1 mg/kg) for seven days. All mice were subjected to three behavioral tests: Morris maze test (for spatial memory), Y-maze test (for spatial memory) and new object recognition test (for non spatial memory). Data for each behavioral test was collected and mice were immediately sacrificed by cervical dislocation and decapitation. Then three brains of each group were collected for histopathological analysis using routine stain (H& E) satin and special stain for amyloid β 1-42 (cogno red stain) and other remaining brains from each group collected for biochemical analysis for A β 1-42 as an Alzheimer's biomarker and BDNF as neuroplasticity parameter and assay of TNF-

α , iNOS , nNOS and NOx as inflammatory biomarkers also assay of MDA , GSH, SOD and NT as biomarkers for oxidative stress.

The results of the present study can be summarized as follows:

Effects of LPS (0.8 mg/kg i.p) includes the following:

- Spatial memory was significantly decreased when compared with normal control group.
- Non- spatial memory was significantly decreased by when compared with normal control group.
- Deposition of A β 1-42 in brain cortex, hippocampus and cerebellum was significantly increased by LPS injection.
- Inflammatory biomarker including : TNF α, iNOS, nNOS and NOx were significantly increased by LPS injection
- Significant decrease in BDNF as neuroplasticity biomarker by LPS injection.
- Oxidative stress parameters as MDA and NT were significantly increased while GSH and SOD were significantly decreased by LPS injection.

Effects of Tempol (100 mg/kg i.p) on LPS induced AD includes the following:

- Spatial memory was significantly increased when compared with LPS group.
- Non-spatial memory was significantly increased by Tempol injection.
- Deposition of A β 1-42 in brain cortex, hippocampus and cerebellum as an Alzheimer's biomarker was significantly decreased.
- Significant increase in BDNF as neuroplasticity biomarker

- Inflammatory biomarker including: TNF α, iNOS, nNOS and NOx were significantly decreased.
- Oxidative stress parameters as MDA and NT were significantly decreased while GSH and SOD were significantly increased.

Effects of telmisartan (0.5 mg / kg) on LPS induced AD include the following:

- Spatial memory was significantly increased when compared with LPS group.
- Non-spatial memory was significantly increased by telmisartan injection.
- Deposition of A β 1-42 in brain cortex, hippocampus and cerebellum as an Alzheimer's biomarker was significantly decreased.
- Significant increase in BDNF as neuroplasticity biomarker.
- Inflammatory biomarker including: TNF α, iNOS and nNOS were significantly decreased also NOx was significantly decreased even it was compared with group received tempol.
- Oxidative stress parameters as MDA and NT were significantly decreased while SOD was significantly increased also GSH was significantly increased even when compared with tempol treated group.

Effects of telmisartan (0.1 mg/kg) on LPS induced AD include the following:

- Spatial memory was significantly increased when compared with LPS group.
- Non-spatial memory was significantly increased by Telmisartan injection.

- Deposition of A β 1-42 in brain cortex, hippocampus and cerebellum was significantly decreased when compared with LPS group, Tempol treated group even with the other dose of telmisartan.
- Significant increase in BDNF as neuroplasticity biomarker when compared with LPS group and the other dose of telmisartan.
- Inflammatory biomarker including: TNF α was significantly decreased when compared with LPS group and tempol treated group, iNOS was significantly decreased when compared with LPS group and the other dose of Telmisartan treated group , nNOS and NOx were significantly decreased when it was compared LPS group , tempol treated group and even with the other dose of telmisartan.
- Oxidative stress parameters as MDA and NT were significantly decreased when compared with LPS group, tempol treated group and the other dose of telmisartan treated group while SOD and GSH were significantly increased when compared with LPS group, tempol treated group and the other dose of telmisartan treated group.

Depending on the results of the current study, it can be concluded that tempol and the two doses of telmisartan enhance spatial and non spatial memory, reduced Aβ 1-42, and increased BDNF also they decreased inflammatory biomarkers as TNF-α, iNOS, nNOS and NOx ,They also decrease MDA, NT while they increased GSH and SOD as an oxidative stress biomarkers when compared with LPS received group.

These finding suggest that lower dose of telmisartan (0.1 mg/kg) showed a significant decrease in Aβ deposition coupled with a significant increase in BDNF content, also administration of telmisartan (0.1 mg/kg) showed a significant decrease in MDA and NT content while showed a significant increase in GSH and SOD content as oxidative stress parameters, concerning inflammatory parameters as TNF-α, iNOS, nNOS, NOx telmisartan (0.1 mg/kg) showed a significant decrease in their contents when compared with the other dose of telmisartan (0.5 mg/kg).

These findings suggest that telmisartan as an angiotensin II receptor blocker especially in lower dose could slow down the progression of the symptoms of AD in a better way than that of tempol treatment.

We suggest that further clinical studies should be conducted on these drugs.