Renoprotective Role of 4-Phenylbutyrate Against Fatty acid-Induced Endoplasmic Reticulum Stress And Cell Death

Shankar Munusamy, MS (Pharm), PhD
Assistant Professor, College of Pharmacy, Qatar University
27 October 2014

Endoplasmic Reticulum (ER) Stress

Markers of ER Stress
- GRP78
- CHOP
- XBP-1
- Free fatty acids
- Albumin
- Glucose

Obesity & End-Stage Renal Disease (ESRD)

Obesity causes renal injury through mechanisms in addition to hypertension and diabetes.

Obesity in Qatar

Obesity, ER Stress and CKD

Objective: To test whether 4-PBA offers protection against FFA induced ER stress and cellular injury in renal cells.
Methods

- NRK-52E (Rat Kidney Proximal Tubule) cells were divided into 4 groups.
- Western blotting
- Trypan Blue Exclusion Assay
- ER Stress Markers (GRP78 & CHOP)
- 24 h Luminometry
- Caspase-3/7 Activity (Apoptosis)

Results: Standardization of In Vitro Model

![Graph showing cell viability with different concentrations of palmitic acid (PA) for 24 h.](image)

Results: Cell Viability

![Bar graph showing cell viability comparison with Vehicle-treated (Control).](image)

Results: ER Stress – GRP78 Expression

![Graph showing GRP78 expression with Vehicle-treated (Control).](image)

Results: ER Stress – CHOP Expression

![Graph showing CHOP expression with Vehicle-treated (Control).](image)

Results: Apoptosis- Caspase-3/7 Activity

![Graph showing caspase-3/7 activity with Vehicle-treated (Control).](image)
Summary and Conclusions

- Exposure of NRK-52E cells to PA resulted in –
  - Significant decrease in cell viability (Renal Cell Death)
  - Induction of ER stress markers (GRP78 and CHOP)
  - Increased caspase-3/7 activity (Apoptosis)
- 4-PBA treatment protected cells from PA-induced ER stress and (apoptotic) cell death.
- 4-PBA acts as “nephroprotectant” and prevents fatty acid-induced ER stress and apoptosis in renal cells.
- Further studies in vivo are required to validate the therapeutic potential of 4-PBA to prevent the development of CKD during obesity.

Acknowledgements

- PHAR445 and PHAR545 Students
  - Dania Alkhiyami
  - Atefeh Moeinzadeh
  - Souad Berzou
  - Hebatalla Mohamed
- Technical Support:
  - Alaaedin Saleh, M.Sc.
  - Dr. Ali Eid
  - Dr. Fatima Mraiche
- Financial Support: Office of Academic Research, Qatar University (#QUST-CPH-FALL-12/13-6 and #QUST-CPH-SPR-12/13-3).