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4-Phenylbutyrate protects renal proximal tubular cells from palmitic acid-induced endoplasmic reticulum stress and cell death

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Obesity is implicated as a significant risk factor for chronic kidney disease (CKD). High plasma free fatty acid levels observed with obesity impairs the endoplasmic reticulum (ER) and cause ER stress. Chemical chaperones, which relieve ER stress, such as 4-phenylbutyrate (4-PBA) have been shown to protect the liver and pancreas against obesity-induced organ damage; however, their protective role in obesity-induced renal damage is unknown. Thus, we investigated the nephroprotective role of 4-PBA in an *in vitro* model of palmitic acid (PA)-induced ER stress and renal injury using normal rat kidney cells (NRK-52E). Cells were divided into four groups: Control, 250 μM PA-treated, 5 mM 4-PBA-treated, and 4-PBA+PA co-treated. After 24 h of PA and/or 4-PBA treatments, cell viability and caspase-3/7 activity (a marker of apoptosis) were determined. Immunoblot analyses were performed to quantitate the levels of ER stress markers - glucose-regulated protein (GRP78) and C/EBP homologous protein (CHOP) - in renal cells. Exposure to PA significantly reduced the viability (81.3% to that of control) in NRK-52E cells, and markedly increased the activity of caspase-3/7 activity (2-fold increase over control) and the expression of ER stress markers GRP78 and CHOP (1.6 and 2 folds over control respectively) at P-value <0.05. Intriguingly, cells treated with 4-PBA were protected from PA-induced ER stress and apoptotic cell death. Our studies demonstrate that 4-PBA acts as nephroprotectant and prevents fatty acid induced ER stress and apoptosis in renal cells. Further investigations *in vivo* are required to validate the therapeutic potential of 4-PBA to protect the kidney and prevent the development of CKD during obesity.

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Controlled release ocular nanosuspension of acyclovir ophthalmic delivery

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The aim of this study is to formulate a novel ophthalmic nanosuspension (ONS), an alternative carrier system to traditional colloidal carriers for controlled release (CR) of acyclovir (ACV). In the present study, ONS is employed to avoid some of major disadvantages of colloidal carriers systems such as instability in cul de sac and short half life by increasing efficiency of drug encapsulation as well as by CR. A quassi-emulsion solvent evaporation method was used to prepare ACV loaded Eudragit RS 100 ONS with the aim of improved ocular bioavailability and distribution. Five different formulations were prepared and evaluated for pH of ONS, particle size, entrapment efficiency, differential scanning calorimetry (DSC), *in vitro* release profile, *in vivo* release studies and stability studies. An average size range of 100 to 300 nm in diameter was obtained and encapsulation efficiency up to 95.0% was observed. *In vivo* studies showed that ACV concentration in aqueous humor at 8 h was 82.83, 77.49 and 34.15 mg/ml. Stability studies showed a maximum drug content and almost similar *in vitro* release compared to the initial data found for the sample stored at 4°C. Overall, the study also revealed that ONS was capable of releasing the drug for a prolonged period of time and increased bioavailability.

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