

2nd International Summit on **Clinical Pharmacy**

December 02-03, 2014 DoubleTree by Hilton Hotel San Francisco Airport, USA

Hepatic tissue bioenergetics is preserved when treated *in vitro* with atorvastatin

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The anti-hyperlipidemic agent, Atorvastatin (3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitor), is commonly prescribed for its potent cholesterol lowering effects. However, elevated transaminases and potential hepatotoxicity are known adverse effects. This study investigated the *in vitro* effect of this agent on hepatic tissue respiration, ATP content, caspase activity, urea synthesis and histology. Liver fragments from Taylor Outbred and C57Bl/6 mice were incubated at 37°C in Krebs-Henseleit buffer continuously gassed with 95% O₂:5% CO₂ in the presence and absence of atorvastatin. Phosphorescence O₂ analyzer that measured dissolved [O₂] as a function of time was used to monitor cellular mitochondrial O₂ consumption. The caspase-3 substrate *N*-acetyl-aspartyl-glutamate-7-amino-4-methylcoumarin was used to monitor caspase activity. The rates of hepatocyte respiration ($\mu\text{M O}_2 \text{ min}^{-1} \text{ mg}^{-1}$) in untreated samples were 0.15 ± 0.07 (n=31). The corresponding rates for samples treated with 50 nM (therapeutic concentration), 150 nM or 1.0 μM atorvastatin for ≤ 13 h were 0.13 ± 0.05 (n=19), $p=0.521$. The contents of hepatocyte ATP ($\text{pmol}^{-1} \text{ mg}^{-1}$) in untreated samples were 40.3 ± 14.0 and in samples treated with 1.0 μM atorvastatin for ≤ 4.5 h were 48.7 ± 23.9 ($p=0.7754$). The concentrations of urea (mg/dL mg^{-1} , produced over 50 min) for untreated samples were 0.061 ± 0.020 (n=6) and for samples treated with 1.0 μM atorvastatin for ≤ 6 h were 0.072 ± 0.022 (n=6), $p=0.3866$. Steadily, hepatocyte caspase activity and histology were unaffected by treatments with up to 1.0 μM atorvastatin for ≤ 6 h. Thus, the studied murine model showed preserved hepatocyte function and structure in the presence of high concentrations of atorvastatin.

Biography

Ali S Alfazari has completed his undergraduate medical degree at the United Arab Emirates University in 1999. He then pursued a formal clinical residency program in internal medicine and then gastroenterology at Dalhousie University, Halifax, NS and University of Ottawa, Ottawa, ON respectively. He is an assistant professor of medicine at the United Arab Emirates University's Department of Medicine and attending physician in the Department of Medicine at Tawam Hospital, Al Ain, United Arab Emirates. His research interests are clinical toxicology and cancer biology.

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