Anti oxidant and apoptotic activities of sitagliptin

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Abstract

Background: Hepatocellular carcinoma (HCC) is the most common and aggressive
type of liver cancer. Most chemotherapeutic medications nowadays imply oxidative stress leading to toxicity, which raises the necessity to find agents with better safety profiles against normal cells in addition to their anticancer activity. Sitagliptin has been shown to possess antioxidant as well as apoptotic properties by the specific suppression of dipeptidyl-peptidase 4, a glycoprotein produced in many tissues that have been thought to promote tumorigenesis
and metastasis.

Methods: Five groups of cell-lines were
included: Control (untreated HepG2 cells); cisplatin treatment HepG2 cells; sitagliptin treated HepG2 cells; combination of different concentrations of cisplatin plus sitagliptin (250 µg/ml) treated HepG2 cells, and finally, combination of different concentrations of sitagliptin plus cisplatin (25 µg/ml) treated HepG2 cells. Then after incubation period for 48 hours, the supernatants were collected to assess malondialdehyde (MDA) and B-cell lymphoma-2 (BCL-2) by ELISA assay kits. Data were finally gathered and analyzed statistically.

Results: Our findings indicated that
sitagliptin decreased significantly the oxidative stress, particularly at high concentrations, through decreasing the MDA level. In addition, sitagliptin exhibited significant apoptotic activity against HepG2 cells through decreasing BCL-2 level. In combination with cisplatin, sitagliptin significantly
potentiated the apoptotic effect and reduced the oxidative stress parameters.

Conclusion: Sitagliptin showed
apoptotic and antioxidant activity against HCC which may potentiate chemotherapeutic agents like cisplatin, in addition to, reduce the oxidative stress against normal cells.

1 The cell were cultured into a 96-well plate with RPMI-1640 and then incubated for 24 hours

2 The old medium was discarded and 200 µL of medium containing the test medicines was added

3 Five primary groups were utilized including the control group, which were: control group, cisplatin-treated HepG2 group, sitagliptin-treated HepG2 group, group that received a different concentrations of cisplatin plus fixed concentration of sitagliptin (250 mcg) and group that received a different concentrations of sitagliptin plus fixed concentration of cisplatin (25 mcg)

4 the plates were incubated for 48 hours

5 the supernatant from each well was collected and frozen at -20 c

6 The MDA and BCL-2 levels were measured by specific ELISA assay kits