عنوان مقاله:

Metformin synergistically increases the anticancer effects of lapatinib through induction of apoptosis and modulation of Akt/AMPK pathway in SK-BR۳ breast cancer cell line

محل انتشار:

مجله علوم پایه پزشکی ایران, دوره 24, شماره 11 (سال: 1400)

تعداد صفحات اصل مقاله: 9

نویسندگان:

Davood Neamati - *Department of Clinical Biochemistry, School of Medicine, Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran*

Azam Khedri - *Department of Clinical Biochemistry, School of Medicine, Ahvaz Jundishapur University of Medical Sciences,Ahvaz, Iran*

Mohammad Aberomand - *Toxicology Research Center, Department of Clinical Biochemistry, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

Ali-Asghar Hemati - *Medicinal Plant Research Center, Department of Toxicology, School of Pharmacy, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

Maryam Mohammadzadeh - *Translational Ophthalmology Research Center, Tehran University of Medical Sciences, Tehran, Iran*

Kourosh Akbari Baghbani - *Department of Infection, Immunity and Inflammation, University of Leicester, LE۱ ۷RH, UK*

Ghorban Mohammadzadeh - *Hyperlipidemia Research Center, Department of Clinical Biochemistry, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

خلاصه مقاله:

Objective(s): Combination chemotherapy is a beneficial intervention for breast cancer, versus single therapy. We investigated the effect of Metformin (Met) on Lapatinib (Lap)-induced apoptosis in SK-BR۳ cells. Materials and Methods: Toxic effect of Met and Lap on SK-BR۳ cells was measured using MTT assay. Flow cytometry was used to measure the co-treatment effect of Met on lapatinib-induced apoptosis. The relative expression of Bax, Bcl۲, and P۲۱ was measured using a real-time PCR. The activity of caspase ۳ and ۹ was measured using an ELISA kit. The protein level of AMPK and Akt was determined using Western blot analysis.Results: Metformin and lapatinib alone and combined form showed significant time- and dose-dependent toxic effects on SK-BR۳ cell viability. The greatest synergistic inhibitory effect on the cell viability [combination index (CI) = ۰.۵۱] was remarkable at Met ۱۰۰ mM combined with Lap ۱۰۰ nM. The combination has a stronger apoptotic death (۴۶%) versus lapatinib alone. The combination considerably increased the mRNA expression of Bax and P۲۱, and caspase ۳ and ۹ activity, while, decreasing the mRNA expression of Bcl۲. Additionally, the combination significantly up-regulated and down-regulated the protein levels of AMPK and Akt, respectively.Conclusion: The metformin-lapatinib combination can induce more potent apoptotic death versus each compound individually. The combination may be suggested as a valuable therapeutic

intervention in patients with breast cancer. However, additional in vivo studies are necessary to evaluate the clinical use of the combination for induction of apoptosis and its antitumor effects.

کلمات کلیدی:
Akt, AMPK, Apoptosis, Drug synergism, Lapatinib, Metformin