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Metformin inhibitory function on tumor cell induce by hypoxia

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Background: The formation of the hypoxic acidic in tumor is an important factor of invasion and metastasis. Although it has been reported that metformin acts as a proliferation inhibitor and apoptotic elevator in cancer cells, the role of metformin in low oxygen supplies has not been yet identified. In line with the differences in oxygen supplies in cancer cells compared to normal cells, in this current study we provided both hypoxia and normoxia condition in order to evaluate the actual anticancer effects of metformin on cancer cells.

Material and method: Normal cells (HEK239) and cancer cells (MCF-7) in both hypoxia and normoxia condition were cultured and treated with different concentrations of metformin. Their proliferation, apoptosis, and necrosis rate assessed using MTT test and annexin V assay. The phosphorylation rate of S6K1 assessed using western blotting. Zymography and western blot were used to measure the expression levels of MMP-9.

Results: Metformin inhibits proliferation more effectively in hypoxia condition compared to normoxia in cancer cells, while it has no significant difference between normoxia and hypoxia conditions in normal cells. Statistical analysis indicates that metformin causes an increase of apoptosis rate in cancer cells with hypoxia condition (p value <0.05), while there is no acceptable increase in normal cells. In addition metformin cause a significant decrease in S6K1 phosphorylation and activation in cancer cells under hypoxia condition compared to normoxia. But there was no significant difference between normoxia and hypoxia condition in normal cells. It also leads to a significant decrease in MMP-9 expression levels more effectively in hypoxia condition compared to normoxia.

Conclusion: Our results indicate that in hypoxia condition metformin exerts its anti-cancerous function by inhibiting proliferation and tumor progression and inducing cell apoptosis more effectively than normoxia condition.

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5-Lipoxygenase and phospholipase A2 inhibitory piperine as anti-inflammatory and anticancer agent

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Piperine is an alkaloid responsible for the pungency of black pepper and long pepper. It has also been used in some forms of traditional medicine. Piperine was discovered in 1819 by Hans Christian, who isolated it from the fruits of *Piper nigrum*, the source plant of both the black and white pepper grains. Piperine is alkaloid, have been reported for various medicinal properties including antimicrobial, anti-inflammatory and anticancer activities. In present study, we have screened isolated piperine for 5-LOX and PLA2, which have important role in inflammatory related diseases and cancer. Piperine showed significant 5-LOX inhibition and moderate PLA2 inhibition in cell free system. Thus, further investigations are needed to develop piperine or its analogs as anti-inflammatory and anticancer agent(s). Acknowledgement: Govinda Rao Duddukuri, Y.Nagendra sastry, Kaladhar DSVGK are thankful to UGC-MRP (F.No. 42-643/2013) for financial support in antiPLA2 studies.

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