PHARMA Pharmacologia

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News & Comments

Impact of Two Enzymes 'G6PD and DHFRse' in Cancer Cell Development

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Hepatoma, or liver cancer, is a type of cancer that develops in the liver. Secondary liver cancer is cancer that has spread to the liver from somewhere else. Every cell has proto-oncogenes, which are cancer-causing genes that are dormant. These proto-oncogenes can be awakened by a variety of triggering agents (chemical, physical, or biological) that modify and turn them into oncogenes; these triggering agents are known as carcinogens. Various innovative approaches for the treatment of liver cancer, such as epidermal growth factor receptors [gefitinib, erlotinib], antibodies targeting Haemoglobin derived Growth Factor (HGF) (bevacizumab), and target tyrosine kinase Furthermore, platinum-based compounds are used in a variety of pharmacological regimens and are the mainstay of treatment. Primaquine inhibits G6PD, which has been confirmed in patients with G6PD deficiency and a higher risk of acute intravascular haemorrhage. The purpose of this study was to see how G6PD and DHFR affected DENA-induced hepatocarcinogenesis in rats.

All experimental procedures were carried out at the Department of Pharmacology, Pharmacology and Toxicology Laboratory, College of Pharmacy, Jouf University, Aljouf, KSA. SYBR1 Green Master Mix (Applied Biosystems, UK), Trizol Reagent (Life Technologies, Grand Island, USA), Primary and secondary antibodies (Santa Cruz Biotechnology, TX, USA) and Membrane LV PVDF (ImmunoBlot-1) with filter paper (Bio-Rad Laboratories, USA) were used. When evaluating risk-benefit ratios, chemiluminescent HRP from (EMD Millipore, USA) still lacks specificity and is more related to toxicities. A total of 30 Albino Wistar rats (6-7 weeks) were obtained from the College of Pharmacy's animal care section at Jouf University in Saudi Arabia. Throughout the research methodology, the animals were kept at ideal humidity levels of 45-55%, a light/dark cycle of 12:12 hrs, and a temperature of 242 degrees Fahrenheit, and were fed a regular pellet diet and water ad libitum.

Rats were randomly assigned to one of five groups (n = 6): Normal Saline (NS) was served to Group 1 for 21 days as a control group. DENA (200 mg kgG1, intraperitoneally [i.p.], single dosage) was given to Group 2, which was identified as a hazardous group. The treatment groups, Groups 3, 4, and 5, were given DENA as directed in Group 2 and were given primaquine methotrexate and a primaquine combination for 21 days. Blood samples were taken using light ether anaesthesia on the final day of the study, and animals were slaughtered after blood was collected using the cervical dislocation method.

In DENA-induced cancer in rats, combined therapy with G6PD and DHFR inhibitors (Primaquine Methotrexate) produces consistent and excellent results. DENA is a hepatotoxin that has been shown

to harm hepatocytes in animal models. The severity of hepatocyte injury was determined by using blood markers (" "DENA-exposed animals had elevated levels of fetoprotein, ALP, ALT, and AST. Serum concentrations are higher "The malignant status of -fetoprotein is further supported by western blot analysis of inflammation-induced proteins.

DENA given to experimental rats induces a considerable increase in blood AST, ALT, LDH, and "-fetoprotein levels, according to the results of this research methodology.

Treatment with methotrexate and primaquine alone or in combination reduced these high levels to normal levels, with the greatest efficacy seen in animals treated with methotrexate and primaquine together.

The lack of selective medications for the treatment of HCC, as well as the potential side effects of current combination therapy, paves the way for the development of more selective and efficacious pharmacotherapeutic regimens for HCC. The current study found that treatment regimens containing methotrexate (a dihydrofolate reductase inhibitor) and primaquine (a glucose6-phosphate dehydrogenase inhibitor) are more effective in preventing the de-novo production of DNA nucleotides.

JOURNAL REFERENCE

Alharbi, K.S., M. Afzal, I. Kazmi, S.I. Alzarea and N.H. Alotaibi et al., 2022. Protective effect of glucose-6-phosphate dehydrogenase and dihydrofolate reductase against diethylnitrosamine-induced hepatocellular carcinoma in rats. Int. J. Pharmacol., 18: 354-362.

KEYWORDS

G6PD, DHFRse, Hepatoma, DENA-induced hepatocarcinogenesis, rats, methotrexate, primaquine, de-novo production of DNA nucleotides