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News & Comments

The Use of Methotrexate, a Dihydrofolate Reductase (DHFR) Inhibitor, can be Very Harmful

Muhammad Sajid

A dihydrofolate reductase (DHFR) inhibitor and structural counterpart of folic acid is methotrexate (MTX). It is a commonly used anti-cancer substance for solid tumours, severe psoriasis, and human leukaemia. The organism's antioxidant system has a balanced defence against reactive oxygen species (ROS) and ROS. An imbalance between the generation of free radicals and the antioxidant defence mechanism is known as Oxidative Stress (OS). It is well known that practically all medications work on the body by affecting enzyme activity. Drug-targeted enzymes are those that work in this way. In light of the aforementioned facts, the current study sought to examine the inhibitory impact of methotrexate, a common anticancer medication, on human PON1.

Erzincan Mengücek gazi Research Hospital provided samples of human serum. At pH 8.0 in 100 mM, tris buffer at 37 degrees Celsius, PON1 activity for paraoxon (diethyl p-nitrophenyl phosphate) was measured. At various medication doses, the enzyme's paraoxonase activities were examined. Using standard polynomial regression software, the mathematical link between the PON1 activity and inhibitor concentration was discovered.

This study looked at how methotrexate affected the activity of the paraoxonase enzyme in vitro. Plotting % activity-[Methotrexate] graphs using five different inhibitor concentrations at a constant paraoxon concentration allowed researchers to calculate the IC50 value for methotrexate, which inhibits PON1. Methotrexate was a very powerful inhibitor and inhibited the PON1 enzyme at very low concentrations. Drug development and discovery have tremendously benefited from the evaluation of enzyme activity in vivo or in vitro. The authors also claimed that lornoxicam, diclofenac sodium, and lincomycin have uncompetitive inhibition mechanisms, while indomethacin, tenoxicam, and ketoprofen have competitive inhibition mechanisms. The findings showed that PON1 was severely inhibited by the medicines employed in the studies, despite their therapeutic doses.

It was concluded as a result that modifying the dosage of this medication is an essential requirement for every patient. Less PON1 produced when a person has low HDL levels. This may result in several ailments, including atherosclerotic plaques and coronary artery disease. The easiest method to prevent medicine side effects is to stick to the specified dosage or to wait to take the medication unless there

are major symptoms.

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KEYWORDS
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