Original Article

Effect of 1,3-Oxazepine Derivative on Alkaline Phosphatase and Lactate Dehydrogenase Activity in Healthy Iraqi Females Serum

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Abstract:

Background: Heterocyclic compounds and its derivatives have biological activities and used as analgesic, anti-helminthic, antituberculer, antifungal, antiviral, anticancer and inhibitor of some enzymes. Oxazepine (benzodiazepine) derivative used in relief of psychoneuroses characterized by anxiety and tension. Alkaline phosphatase (ALP) hydrolyzes phosphate monoesters, while Lactate dehydrogenase (LDH) catalyses oxidation of L-lactate to pyruvate utilizing NAD+

Objective: The study was carried out to know of the impact of 1,3-oxazepine derivative on the ALP and LDH enzyme activity on human serum in vitro.

Methods: The study included the effect of synthesized 1,3-oxazepine divertive [(Z)-3-(5-mercapto-1-3,4-Thiadizol-2-yl)-2-(4-nitrophenyl)-2,3-dihydro-1,3-oxzepine-4,7-dione] on the activity of enzymes ALP and LDH for (34) healthy Iraqi females serum in vitro. The activity of both enzymes was measured spectrophotometrically. Different concentrations of 1,3-oxazepine derivative were used and the inhibition percentage was calculated.

Results: The results of this study revealed that effect of 1,3-oxazepine derivative was inhibitor for ALP and LDH activity and the high inhibition percentage was 87.56% for ALP. The high inhibition percentage was 50% for LDH when 1,3-oxazepine derivative was used.

Conclusions: 1,3-oxazepine derivative affected as inhibitor on ALP and LDH enzyme activity in human serum in vitro. This can be used in drug industry in the future.

Key wards: Alkaline phosphatase, Lactate dehydrogenase, 1,3-oxazepine derivative.

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Introduction:

Alkaline phosphatase (ALPs)(EC 3.1.3.1) is a group of enzymes that hydrolyze organic phosphate at alkaline pH. ALP has many isoenzymes encoded by different genes(1). They are present in most tissues of the body in particularly high concentration in intestinal epithelial cell, kidney tubules, bone, liver and placenta(2). The ALP measurements give total serum activity without specificity to its source(3). The ALP function is osteogenic activity in bone mineralization(4). Moreover, ALP regulates lipid transport(5).

Lactate dehydrogenase (LDH) (EC 1.1.1.27) is an oxidoreductase tetrameric enzyme exists as five isoenzyem. LDH is highly expressed in smooth muscle tissue(6). LDH catalyzes reduction of the keto group in pyruvate to the hydroxyl group yielding lactate due to the oxidation of NADH to NAD^+ in the last step of glycolysis(7,8) Heterocyclic organic compounds have an important role in pharmaceutical field due to their biological activities such as anti-inflammatory, antimicrobial and antidyslipidimia effects(9,10). Oxazepine compounds are listed on the pharmaceutical benefits scheme and having anti-convulsant, muscle relaxant, sedative and amnesic properties(11,12).

1,3-Oxazepine derivatives are seven member heterocyclic ring which contain two hetero atom (oxygen and nitrogen) in their structure,. These derivatives have been studied and reported in variety biological prosperities such as antimicrobial and inhibitors of apoptosis proteins (IAPs) activity that led to use them in treatment of cancer(13,14)

The aim of this study is to assess the effect of 1,3-oxazepine derivative on ALP and LDH activities in Iraqi healthy female serum in vitro.

Subjects, Material and Methods:

The subjects were thirty four healthy Iraqi females with age (20-45) years. The Fasting blood sugar and lipid profile for the subject were normal value when they attended medical city of Baghdad during the period November 2014- January 2015.

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Five milliliters of fasting blood were collected from these subjects. The serum obtained used in determination of ALP and LDH were with normal values.

The synthetic1,3-oxazepine derivative that used in this study was prepared in previous study(15). The structure of 1,3-oxazepine derivative is shown in figure (1).

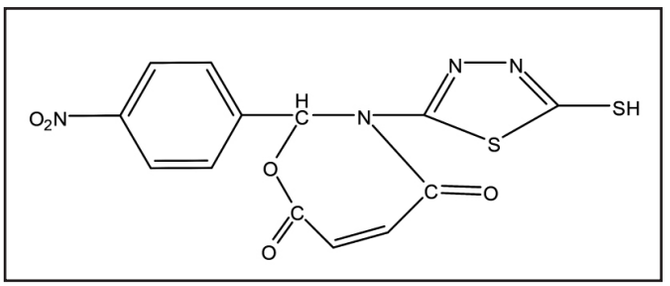

Figure (1): The structure of 1,3-oxazepine derivative(15)

The ALP activity was determined by using the ready kit from Biosystems, and recording the absorbance at 405 nm. LDH activity was measured by suing ready kit from Worthington Biochemical Corporation, and the absorbance was measured at 340nm.

Five different dilutions (10^{-2}, 10^{-3}, 10^{-4}, 10^{-5} and 10^{-6} M) for the 1,3-ozaxepine derivative were prepared from the stock solution (10^{-1} M) in distilled water with addition of few drops of ethanol. Activities of ALP and LDH were determined before and after addition of different concentrations of the 1,3-oxazepine derivative. The inhibition percentage was determined by using different concentration of the prepared organic compound with fixed concentration of substrate. The activity of the enzymes without addition was considered to be 100% and the results were relative to it.

Results:

The 1,3-oxzaepine derivative showed inhibitory effect on both enzymes ALP and LDH activity (87.65% and 50%) respectively. The results revealed that highest inhibition percentage was performed by using a 10^{-2} and 10^{-6} M of 1,3-oxazepins derivative for ALP and LDH respectively. The table below shows the data obtained.

Table: Inhibition percentage for APL and LDH enzymes

Molar Concentration of 1,3-oxzaepine derivative	% inhibition*	
	ALP	LDH
10^{-2}	36.32	50.00
10^{-3}	40.64	22.69
10^{-4}	58.83	13.81
10^{-5}	75.66	10.20
10^{-6}	87.65	10.16

*The % inhibition was mean of all study samples

Discussion:

The synthetic1,3-oxazepine derivatives which prepared by previous study showed inhibitory effect on ALP and LDH activities in healthy Iraqi female in vitro. This could be attributed to the affinity of such compounds to compete on the binding to the active sites of the enzyme. The changes of normal LDH activity were studied in pervious researches by using different concentrations and substances or oxygen stress(16, 17). More recently, natural extracts of commonly used herbs had ability to inhibit LDH subtype A(18)

Previous studies showed that the synthesized oxazepine derivatives had high antibacterial activity against E.coli, S.aureus, Salamonella typhii and moderate activity against Klebsiella pneumonia(19). Others showed highest and low bilological activity against S.aureus and no activity against E.coli(20).

Conclusion:

The activity of ALP and LDH change were affected in presence of 1,3-oxazeoine derivative as inhibitor in healthy serum in vitro, this may be used in the pharmaceutical and drugs industry in future.

Authors Contributions:

Warka'a design and wrote the paper, Anwar study conception, Hassan and Ali collected the sample and the references.

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