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تقييم فعالية GOT في مصل دم الانسان بتأثير الفلاجيل Metronidazole

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أجريت هذه الدراسة مختبرياً لغرض معرفة تأثير التراكيز المختلفة من Metronidazole على نسبة (GOT) في مصل دم الانسان وظهرت النتائج انخفاض في نسبة GOT. اذ وصلت النسبة الى الصفر في كافة التراكيز.

Evaluation of Serum Glutamic Oxaloacetic Transaminase activity by Metronidazole

Abstract

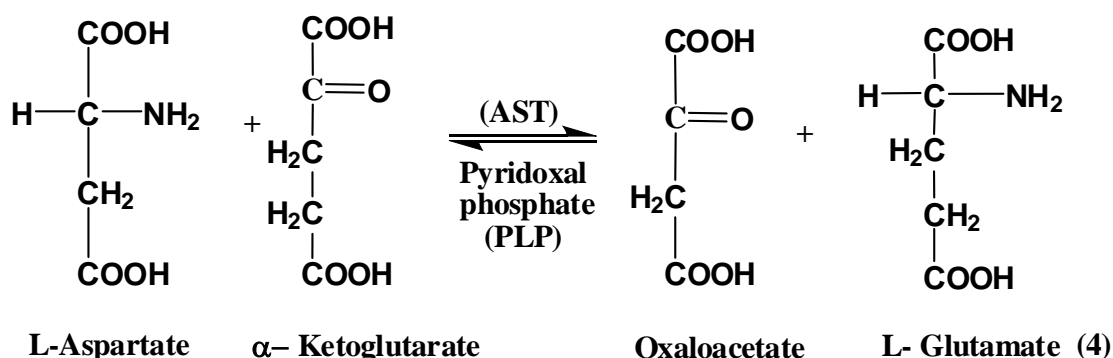
This study has done in vitro to know the effect of different concentration of metronidazole on (SGOT) activity. The result revealed a depression of (SGOT) activity by metronidazole. The (SGOT) activity drop and reaches to zero in all concentration, of the drug under consideration.

Introduction

Serum Glutamate oxaloacetate transaminase (SGOT). Also called aspartate transaminase (AST) present in high concentration in the heart, liver, skeletal muscle, kidney and erythrocytes, damage to any of these tissue, cancer or other diseases may increase plasma GOT activity (1) (2) Very high values > 500 units /L, usually suggest hepatitis or other kinds of hepato cellular necrosis but can also be found with large necrosis tumors, other types of necrosis extensive hypoxia, congestive of failure, and shock. (3)

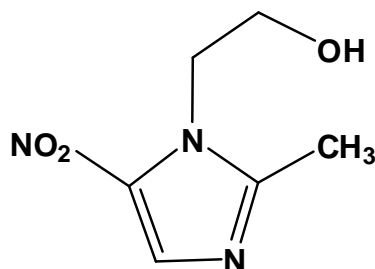
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GOT Catalyase the following reaction



Metronidazole

The chemical name 2-Methyl-5-nitromidazole -1-ethanol
Structural Formuls



Molecular Formula: C₆H₉N₃O₃

Molecular Weight: 171.15

Physical form: white to pale yellow crystal or crystalline powder.

Solubility: sparingly soluble in water and in alcohol, slightly soluble in ether and in chloroform

pKa: 2.6

PH: 5.8 (saturated solution)

Melting point: 159-163°C (5)

Metronidazole, antiprotozoal antimicrobial agent, was first used for treatment of systemic anaerobic infections by Tally et al (6) subsequent studies have shown metronidazole

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to possess excellent in vitro activity against the common anaerobic pathogens (7,8,9)

Action and clinical pharmacology metronidazole is bactericidal against anaerobic bacteria, it exerts trichomonacidal activity and is also active against Gigardia Iamblia and Entamoeba Hislolytica. Its exact mechanism of action has not been entirely determined as yet. It has been proposed that an intermediate in the reduction of metronidazole, produced only in anaerobic bacteria and protozoa is bound to deoxyribonucleic acid and electron transport proteins, inhibits subsequent nucleic acid synthesis.(5)

At present the mechanism by which topical metronidazole reduces the lesions and erythema associated with aone rosacea is not precisely know despite the established antimicrobial effects of metronidazole, there is no evidence that the suppression of bacteria or parasitic mites harbored.(5)

in the skin is directly responsible for its beneficial effects in rosacea. In vitro and in vivo studies indicate that metronidazole has direct anti inflammatory activity and effects neutrophil chemotaxis and cell – mediated immunity. An antioxidant action via inhibition of neutrophil – generated reactive oxgen species has also been demonstrated, this action is believed to underlie its anti inflammatory effect. It has been proposed that the reduction in rosace a lesions and erythema is the result of anti inflammatory or immunosuppressive actions of metronidazole. (5)

The aim of the study

Glutamate oxaloacetate transaminase (GOT) (EC2.6.1.1) is one of the enzymes studied in liver function test and since liver is the sile of detaxification of all drugs so this study focused on the effect of Metronidazole using different concentration of the drug.(10)

Materials and Methods

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1. serum (from healthy people)
2. GOT (BIOMERIEUX/France)
3. Metronidazole (Ankle shwar – India)
4. Spectrophotometer (spectrosc) Labo Medinc.
wave length 505 nm

Colorimetric method used for determination of Glutamic – oxaloacetic transaminase (GOT) in serum.

The effect of different concentration of the drugs were tested on GOT activity in serum with (10^{-2} , 10^{-3} , 10^{-4} , 10^{-5} , 10^{-6} , 10^{-7}) Molar of Metronidazole according to the method (Reimananl Frankel, 1957)(10) as follows:

α - oxoglut + L- aspartate $\xrightarrow{\text{GOT}}$ L- glutamate + oxaloacetate

Results and Discussion

The drug used in this study was liquid the stock solution (10^{-2}) was the drug without dilution. Stock solution (1 ml) was diluted to 10 ml in volumetric flask to give (10^{-3}) M then 10^{-4} , 10^{-5} , 10^{-6} , 10^{-7} M from 10^{-3} , 10^{-4} , 10^{-5} , 10^{-6} M were prepared respectively. The enzyme activity was measured according to the method (11).

In the first experiment, the velocity of uninhibited enzyme was established, in the second experiment, a constant amount of inhibitor used throughout the study, different concentrations of substrate were used. Different substances have the ability to reduce or eliminate the catalytic activity of specific enzyme. (12)

Figure (1) showed the Calibration curve of (SGOT) concentration by plotting absorbance against concentration. The influence of each dilution of the drug were tested on SGOT activity, they are shown in table. (1)

All concentration caused depression of SGOT activity which fail to zero. Metronidazole may interfere with certain types of determinations of serum chemistry values. Such as aspartate amino transferase(13) (14)

Like other amino transferase SGOT contain the prosthetic group pyridoxal phosphate (PLP), which is derived from pyridoxine (vitB6), which is covalently linked to the ϵ -amino

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acid group of specific lysine residue at the active site of the enzyme Amino trans ferases act by transferring the amino group of an amino acid to the pyridoxal part of the coenzyme to generate pyridoxamine phosphate.

The pyridoxamine form of the coenzyme reacts with an α – keto acid to form an amino acid, at the same time regenerate the original aldehyde form of the coenzyme. (15) (16)

In clinical trials during metronidazole therapy the SGOT decreased progressively, reaching nadir of zero IU. (17)

So in our mind that any substance that interferes with the mechanism of action of SGOT might inhibit or diminish the activity of the enzyme as in the present study.

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Compound Conc.	% Activity
10^{-2}	Zero
10^{-3}	Zero
10^{-4}	Zero
10^{-5}	Zero
10^{-6}	Zero
10^{-7}	Zero

Table (1) The effect of each dilution of the drug on SGOT activity.

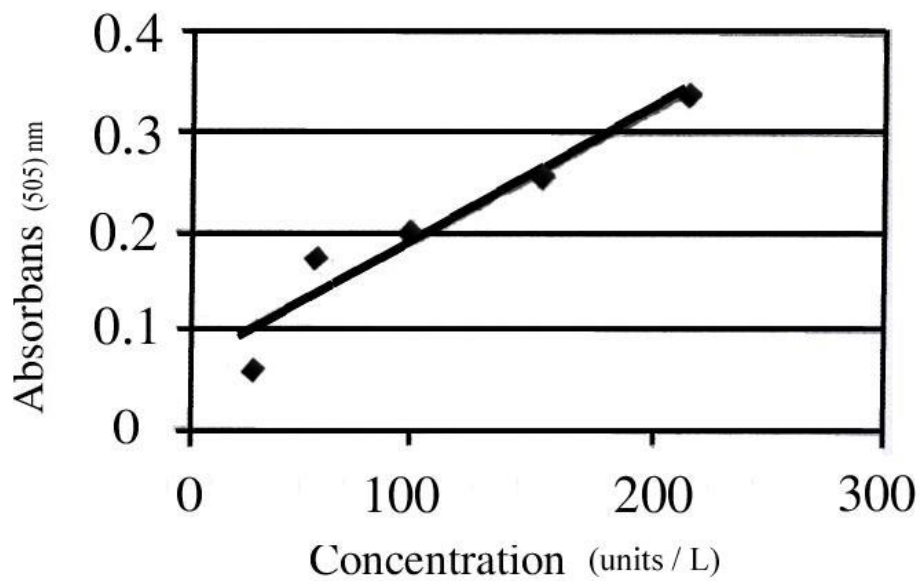


Figure (1) Cabilration Curve of SGOT