

# Drug Interferences in Clinical Analyses

PREVECAL DEPARTMENT

Nº 2

## ALANINE AMINOTRANSFERASE ALT/GPT ( IFCC )

**W**e will analyse in this second Bulletin on the interference of drugs in clinical trials the effects that the most important compounds interfering analytically and physiologically with Alanine Aminotransferase ALT/GPT IFCC method testing cause.

This test is one of those suffering the greater interferences with ALT/GPT being one the main indicators for measuring liver activity. This organ is in charge of processing most medicines and regulate their activity all over the human body. Once a drug is administered, the liver converts it into compounds that can be used efficiently and it is also in charge of eliminating toxic residues that are generated during this transformation. During these processes these chemical compounds can attack and damage the liver. Most interferences are due to the physiological effects of the drugs on modifying the liver's basal metabolism.

### CLINICAL MEANING

Aminotransferases catalyse the formation of glutamic acid from 2-oxoglutarate by transferring amino groups. ALT is found in different tissues although the greatest concentration is found in the liver and kidneys.

High serum ALT concentration are reported in hepatitis and other hepatic disorders associated with necrosis: infectious mononucleosis, cholestasis, cirrhosis, metastatic liver carcinoma, Delirium Tremens, as well as after administering some opiate, salicylate or ampicillin medicines.

High serum ALT concentrations can also be found in skeletal and cardiac muscle disorders.

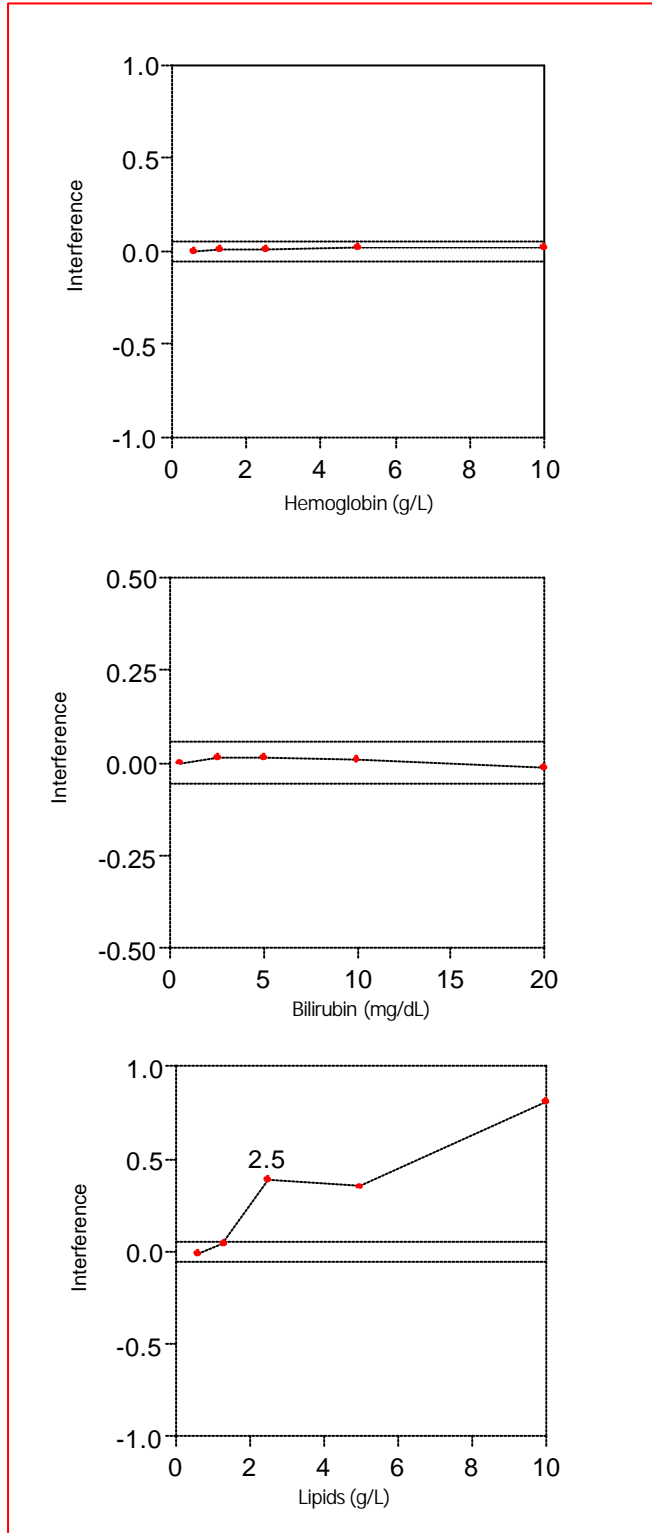
### METHODOLOGY INTERFERENCES

Each point is the average of three. Horizontal lines show the tolerance for the value obtained in the presence of interference, calculated as: the average in the absence of interference  $\pm 3 \times$  interseries standard deviation.



Sample: human serum without (a) and with growing concentrations of interference (b).

Interference:  $(b-a)/a$



Hemolysis (hemoglobin 10 g/L) and bilirubin (20 mg/dL) do not interfere.  
Lipemia (triglycerides 2 g/L) may affect the results. Other drugs and substances may interfere.

## DRUG INTERFERENCES

### ANALYTICAL INTERFERENCES (DECREASE)

#### METRONIDAZOLE

Interference reported with IFCC method, since its absorption peak is similar to NADH's at pH 7. Even zero values reported.

### PHYSIOLOGICAL INTERFERENCES (DECREASE)

#### INTERFERON ALFA 2a

Rapid ALT activity decrease reported in patients with hepatitis C when administered. Average decrease after 6 months of treatment is 62% and in many cases it takes ALT levels to within range of normal values. The decrease in activity is reversible once the treatment is suspended.

#### INTERFERON ALFA 2b

Reduction in serum ALT levels in patients with hepatitis C when administered, in some cases down to normal values, in 70% of patients reported.

#### URSODIOL

Reduction in ALT activity reported in the most common hepatic disorders, especially with cirrhosis patients when administered. This decrease depends on the treatment time (the greater the time, the greater the decrease) and it is reversible when treatment is suspended.

### PHYSIOLOGICAL INTERFERENCES (INCREASE)

#### ANTICONVULSANTS

Increase in serum ALT concentration reported in epileptic patients when administered. The increase can reach 50% of normal values.

#### ACETYLSALICYLIC ACID

Aspirin is hepatotoxic depending on the dose. When the serum concentration is higher than 25 mg/L when administered for more than a week, it provokes hepatotoxicity to an average degree or is reversible.

#### ATORVASTATIN

The serum ALT concentration increases from 1 to 8% when administered.



#### *BISOPROLOL*

Significant enzyme activity (150-200%) reported in 5% of patients when administered.

#### *CARVEDILOL*

Average degree hepatic injuries reported in 1% of hypertense patients when administered.

#### *CYCLOSPORINE A*

Very significant serum ALT concentration increase (130-200%) in patients undergoing bone marrow transplants reported.

#### *DICLOFENAC*

Significant serum ALT concentration increase (3 times normal values) in more than 2% of patients when administered.

#### *ERYTHROMYCIN*

Average hepatotoxicity reported in 15% patients when administered.

#### *STREPTOMYCIN*

Significant serum ALT concentration increase reported in tuberculosis patients when administered and in combined treatments with Isoniazid, Rifampicine and Pyrazinamide.

#### *FLUCONAZOLE*

Reversible increase in the serum ALT concentration reported in 5% of patients when administered. It can lead extraordinarily to serious hepatic injuries.

#### *FLUVASTATIN*

3 times normal value serum ALT reported in 1% of patients when administered.

#### *g-GLOBULIN*

Moderate increase in serum ALT concentration in 25% of primary immunodeficient patients when administered intravenously for more than 6 months reported.

#### *HALOPERIDOL*

Moderate increases in serum ALT concentration in 45% of patients when administered.

#### *IBUPROPHENE*

Hepatic enzymes activity increase in 15% of patients when administered. In 1% of patients this increase can represent three times the normal ALT values.

#### *INTERLEUKINE 2*

Increase of ALT activity can reach 6-7 times normal values in prolonged treatments with cancer patients reported.

#### *ISONIAZID*

Average hepatic injuries in 10% of patients when administered possibly due to the conversion into acetyl hydrazine or some related hepatotoxic compound. This effect increases when administered together with Rifampicine.

#### *LEVODOPA*

Normal ALT activity increase in 17% of Parkinson's patients when 2 months treatment administered. Such increase is reversible when treatment is suspended.

#### *LOVASTATIN*

Marked increase up to 3 times normal serum ALT value in 2% of patients when administered for at least a year. Increase usually occur after 3 months treatment.

#### *NIACIN*

100% serum ALT concentration increase reported for a dose of 1 gr/day when 1 month's treatment administered. Reduction to 50% concentration after 2 months treatment.

#### *ORAL CONTRACEPTIVES*

Significant serum ALT concentration increase when 3 month's treatment administered.

#### *PRAVASTATIN*

Significant serum ALT activity increase (20%) in primary hypercholesterolemic patients when 40 mg/day dose administered for 4 months.

#### *SIMVASTATIN*

Increase reported up to three times the base ALT concentration in 1-3% patients when administered.



## **NON INTERFERING DRUGS**

The following drugs do not interfere at therapeutic concentrations:

Ampicillin, Ascorbic Acid, Bromazepam, Carbamazepine, Chloramphenicol, Diazepam, Enalapril, Gentamicin, Low Molecular Weight Heparin, Lidocaine, Morphine, Penicillin G, Phenobarbital, Quinine, Tetracyclines.



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