INRatio Monitor and Interfering Substances

The International Normalized Ratio (INR), was developed by the World Health Organization in the early 1980s, and is designed to eliminate problems in oral anticoagulant management caused by variability in the sensitivity of different commercial sources and different lots of thromboplastin. The INR is used worldwide by most laboratories performing oral anticoagulation monitoring, and is routinely incorporated into dosage planning for patients.

There are two categories of effects that can influence the INR; those that can affect the therapy itself and those that can affect the Prothrombin Time test used to monitor the therapy.

The first category includes changes in diet, (particularly foods high in vitamin K), alcohol use, other drugs and illness can all affect the INR. These factors require that the INR is monitored regularly so the patient stays within the desired therapeutic range. Some of these factors are discussed in more detail below.

Congestive Heart Failure can cause hepatic congestion of blood flow and inhibit warfarin metabolism.

Hypothyroidism decreases the catabolism of the vitamin K clotting factors. Therefore, hypothyroidism could be suspected if there is a general trend toward decreased INR values, leading to increased warfarin dosage.

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Hepatic failure may significantly elevate the INR due to decreased production of clotting factors.

Vitamin K intake can promote increased production of vitamin K clotting factors, decreasing the anticoagulant response. Alternately, decreased consumption can increase the anticoagulant response.

The foods that contain the highest amounts of Vit.K per serving are green leafy vegetables, such as spinach, broccoli, turnip and greens.

Drugs that inhibit the metabolism of warfarin can increase the INR value. Amidorone for example causes inhibition of breakdown of warfarin in the liver and can increase the INR.

Drugs that induce the metabolism of warfarin can decrease the INR value.[2]

Anticoagulant or anti-thrombotic drugs such as Heparin and Low Molecular Weight Heparin will cause the INR to be higher because they are affecting the coagulation cascade directly.

The second category includes heparin in the sample, anti-phospholipid antibodies in the sample, and hematocrit. The same factors are discussed in more details below.

Heparin in the sample can artificially increase the INR. Samples for Prothrombin Time tests should not be drawn from in-dwelling vascular catheters since these are flushed with heparin which can contaminate the sample.

Anti-phospholipid antibodies can disrupt the phospholipid in the PT reagent that is necessary for the clotting reaction to occur thus artificially elevating the INR.

Hematocrit which is too high or too low can affect the results of some systems that use whole blood samples. Always use these devices within the manufacturers recommended range for hematocrit.

Some of the factors that were tested for interference during limitations studies for the HemoSense INRatio are tabulated below.

Effect of Bilirubin

	10 mg/dL	20 mg/dL
Control (mean)	1.11	1.15
Test (mean)	1.14	1.08
% difference	-2.5%	6.0%

There is <10% interference due to bilirubin up to concentration of 20 mg/dl.

Effect of Hemolysis

	250 mg/dL	500 mg/dL
Control (mean)	0.97	1.00
Test (mean)	0.94	0.98
% difference	-3.0%	-2.3%

There is <10% interference die to hemolysis up to hemoglobin concentration of 500mg/dl.

Effect of Heparin

	4 U/mL	8 U/mL
Control (mean)	1.13	1.09
Test (mean)	1.71	1.40
% difference	51%	28%

Effect of Low Molecular Weight Heparin

	4 U/mL	8 U/mL
Control (mean)	1.02	1.12
Test (mean)	3.02	2.96
% difference	191%	166%

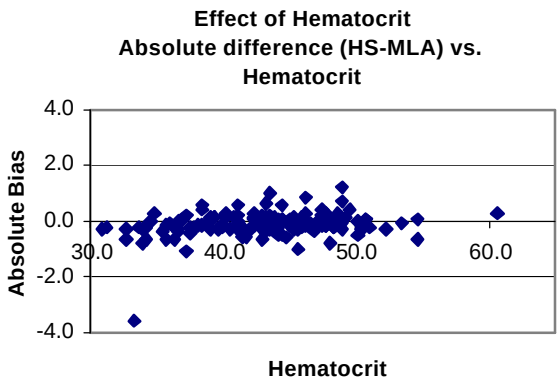
Both standard and low molecular weight heparin cause significant interference in the test results at the concentrations tested. Samples from patients undergoing heparin therapy should not be used for testing on the INRatio system.

Effect of Triglycerides (mg/dL)

	1000	1500	2000	3000
Control (mean)	1.28	1.09	1.09	1.17
Test (mean)	1.10	1.16	1.28	1.30
% difference	-17.4%	7.1%	17.4%	11.4%

There is 10% or less interference due to lipemia up to a triglycerides concentration of 1500 mg/dl.

Effect of Hematocrit



Accurate results were obtained on samples with hematocrits ranging from 30 to 55%.

References:
1. Demirkan K, Stephens MA, Newman KP, Response to warfarin and other oral anticoagulants; effects of disease states. South Med J 2000; 93:448-485.
2. Amir Jaffer, Lee Bragg, Practical tips for warfarin dosing and monitoring. Cleveland Clinic Journal of Medicine, volume 70, number 4, April 2003, p 361-371.

HemoSense

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