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TRYPTOPHAN PYROLYSIS PRODUCTS FOUND IN COOKED FOODS INHIBIT HUMAN PLATELET AGGREGATION BY INHIBITING CYCLOOXYGENASE.
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Humans are exposed to numerous toxic compounds in foods. During the past decade, several carcinogenic heterocyclic amines have been reported to be present in the cooked foods. Recently, we reported that some of the carcinogenic heterocyclic amines isolated from foods were present in human plasma. In order to know the effects of the carcinogens isolated from foods on the cell function, we investigated the effects of the carcinogenic heterocyclic amines including Trp-P-1(3-amino-1,4-dimethyl-5H-pyrido|4,3-b|indole) and Trp-P-2(3-amino-1-methyl-5H-pyrido|4,3-b|indole) on human platelet aggregation and polymorphonuclear leukocyte aggregation. Only tryptophan pyrolysis products, Trp-P-1 and Trp-P-2, had potent inhibitory effects on human platelet aggregation when platelets were preincubated with the carcinogens for 15 min. Other carcinogenic heterocyclic amines such as glutamic acid pyrolysates (Glu-P-1 and Glu-P-2) and 3H-imidazo |4,5-f|quinoline-2-amines(IQ and MeIQ) did show no effect on platelet aggregation even at 100 μM.

Stimulants (final concentration)	IC 50 for human platelet aggregation Trp-P-1 (μM)	Trp-P-2 (μM)
Sodium arachidonate (1mM)	15	25
Collagen (2 μg/ml)	25	43
ADP (5 μM)	35	50

The autoradiogram demonstrated that Tryptophan pyrolysis products,Trp-P-1 and Trp-P-2, dose-dependently inhibited the formation of HHT,PGD_2,PGE_2 and TXB_2 induced by sodium arachidonate in human platelets labeled with |^{14}C| arachidonic acid. Moreover, Trp-P-1 and Trp-P-2 did not show significant effects on leukocyte aggregation induced by sodium arachidonate (0.75mM) even at 100μM. It is concluded that Trp-P-1 and Trp-P-2 isolated from cooked foodstuffs have potent inhibitory effects on the cyclooxygenase pathway of the platelet. Therefore, human platelet function might be affected with daily foods containing tryptophan pyrolysis products in vivo.

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FATTY ACIDS AND PLATELET FUNCTION IN A SOUTH AMERICAN INDIAN GROUP WITH A HIGH DIETARY CONSUMPTION OF DOCOSAHEXAENOIC ACID,
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The effect of dietary polyunsaturated fatty acids on hemostasis has elicited much interest. We studied indians from the Orinoco river shore, whose main animal protein intake derives from river fishes with a high content of 22:6n-3 (0.2g/100g), We determined in 50 indians plasma phospholipid fatty acids (FApl) by gas/liq chromatography and bleeding time by Symplate I divice (BT), in 15 were analyzed platelet count, aggregation with collagen and ADP, platelet factor 3 availability (PF3), platelet phospolipid fatty acids (FApt) and plasma vWFAg.RA from human milk was also determined. Subjets from the city of Caracas served as control. Data on BT, FAlp and FApt are shown in table (X±SD).

	BT min	% 22:6n-3 pl	% 22:6n-3 pt	% 20:4n-6 pl	% 20:4n-6 pt	20:4/22:6 pl	20:4/22:6 pt
Indian	5.7 ± 1.9	6.7 ±1.7	2.7 ±0.4	12.7 ± 2.7	27.2 ±2.9	1.9 ±0.6	12.8 ±1.9
Control	3.1 ± 0.3	2.4 ±1.2	1.9 ±0.4	10.6 ± 2.1	25.1 ±4.0	4.4 ±1.5	13.7 ±3.5
	p< 0.001	< 0.10	< 0.01	NS	NS	< 0.01	=0.05

FA Composition of milk showed that indians have 3 times more 22:6n-3 than controls. Platelet studies showed normal number and morphology. Percent platelet aggregation with collagen (4ug/ml) was below 50% in 4 of indians, 2 of them with a BT within the control range. Maximum slope of aggregation with ADP (4uM) was diminished in 2 cases. Diference in PF3 was not significant, VWFAg range from 50 to 100% and control from 53 to 127%. In conclusion we have found a population that shows an increased plasma and platelet 22:6n-3 and a prolonged BT most likely of dietary origen. Mechanism by wich n-3 FA modifies BT needs further investigation.

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FISH AND PLATELETS
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The effect of two different amounts of a fish oil, corresponding to 0.75 g (2.5 mmol) and 1.5 g (5 mmol) of eicosapentaenoic acid respectively, added in a cross-over design to the normal diet of 16 healthy male volunteers, was studied. Of the various parameters investigated, the most important appeared to be a new test: "Transient Aggregation Resistance" (TAR) of platelets, a phenomenon which, due to its short half life, is hardly measured when platelet aggregation is studied according to the classic method (see M.R.Hardeman, TAR determination, this congress). Under the influence of fish oil, the half life of TAR was found significantly prolonged. This prolongation, however, was not related to the amount of fish oil used. A highly significant decrease of triglycerides was found, the effect being most pronounced in subjects with triglycerides starting values >1.0 uM. This decrease was related to the amount of fish oil used. These results may cast light on controversies found in literature concerning the effect of fish oil on platelet aggregation. They can also help to clarify controversies about the effect of fish consumption on cardiac mortality.

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TRANSIENT AGGREGATION RESISTANCE OF HUMAN PLATELET-RICH PLASMA; A NEGLECTED IN VITRO PHENOMENON WITH PHYSIOLOGICAL IMPACT.
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Due to instability in the first in vitro period, platelet-aggregometry is usually deliberately postponed until ca. 1 hour after venepuncture (VP). At that time aggregability is fairly constant for 1 hour or more. Investigation of the period immediately followed VP, however, revealed a high aggregation resistance - measured as the threshold ADP-concentration which the platelets just could resist before they aggregate maximally and irreversibly - which subsequently decreased exponentially with time. This "Transient Aggregation Resistance" (TAR) appeared to be superimposed on a stable, so called Baseline Aggregation Resistance (BAR). The latter, measurable 60 min or more after VP, yields the "classical" threshold ADP-concentration.
Parallel aggregation-studies started 6 min after VP, subsequent studies were performed every 4 min. pH was controlled during storage of PRP at roomtemperature. Extrapolation of the TAR-curve to t=0 (i.e. time of VP) yields the maximal value:TAR_{max}. Coefficients of variation for TAR_{max}-method: 9.4% (n=6); intraindividual 15% (n=15, over 3 yrs); interindividual: 51% (n=16,wide range).

This TAR-phenomenon which is proven to be caused by a plasma-factor, can be influenced by dietary n-3 fattty acids and can be also inhibited by ASA,suggesting a prostanoid nature. The physiological significance of TAR_{max} can be illustrated by the following findings:1. Patients with myocardial infarction, hyperlipoproteinemia, sickle cell anemia (i.e. diseases with a high risk for thrombotic complications) have low TAR_{max}-values. 2.Individuals with "spontaneous platelet aggregation" in vitro,but asymptomatic, have positive TAR_{max}-values. 3.There is a clear,reciproke age-dependency of TAR_{max}.
It is concluded that a technique is available measuring the effect of circulating,labile platelet-aggregation influencing plasma factor(s). Furthermore, using this technique,it was found that normal fresh plasma contains a labile aggregation-inhibiting factor which is several orders of magnitude more potent than other stabile factors either present in plasma or associated with platelets. This factor is probably of prostanoid nature and might have significance as a reflection of the antithrombotic potential of the endothelium.