MECHANISM OF ACTION OF ASPIRIN ON PLATELET FUNCTION

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Inhibition of platelet aggregation and of the reaction of liberation of platelet factor 3 under the influence of aspirin was shown to be due to the action of the drug not only on the platelets, but also on plasma cofactors: In experiments *in vitro* the blood plasma of rats receiving aspirin reduced the aggregating power of the platelets of intact animals; blood plasma of intact rats increased the aggregating power and accessibility of factor 3 of the platelets of animals receiving aspirin.

KEY WORDS: *aspirin; platelets; blood plasma.*

Aspirin is known to inhibit the second wave of aggregation of platelets and the liberation of platelet factors 3 and 4 [8]. This effect is linked with the direct action of aspirin on the platelets [2, 7]. However, the functional properties of two plasma platelet aggregation cofactors — fibrinogen and an unknown thermostable factor [5] — are disturbed.

This paper gives data on the effect of aspirin on platelet aggregation, on plasma aggregation cofactors, and on the reaction of liberation of platelet factor 3.

EXPERIMENTAL METHOD

Experiments were carried out on Wistar rats weighing 180-200 g. Aspirin, as a 5% suspension in starch gel, was introduced into the esophagus in a dose of 50 mg/kg. In the experiments of series I aspirin or 1% starch gel (control) was given as a single dose, in series II as four doses over a period of 2 days. Under pentobarbital anesthesia blood was taken from the abdominal aorta of the experimental and control animals 24 h after the last dose of aspirin, stabilized with 3.8% sodium citrate (9:1), and subjected to differential centrifugation to obtain fractions of platelet-enriched and platelet-deficient plasma. Platelet-rich blood plasma from the experimental and control rats was diluted with platelet-deficient plasma of the experimental or control animals to a concentration of 300,000 platelets/μl. The four different suspensions of platelets thus obtained (Table 1) were tested simultaneously for aggregation power [1] and for accessibility of factor 3 [3]. The disodium salt of ADP (Serva, Heidelberg) was used as the aggregant in a final concentration of 10^{-5} M (the minimal dose causing two waves of aggregation of the platelet suspension of intact rats). Aggregation of the platelets was expressed as the change in optical density in percent, the difference between optical densities of the palatelet-rich and platelet-deficient plasma being taken as 100%. The accessibility of factor 3 was expressed in seconds of recalcification of a kaolin-treated platelet suspension, and the concentration of salicylates in the blood plasma was determined [4].

EXPERIMENTAL RESULTS

Comparison of the indices for suspensions 1 and 3 (Table 1) shows that administration of aspirin to the animals led to a decrease in the functional properties of the platelets.

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TABLE 1. Changes in Functional Properties of Platelets and Blood Plasma after Administration of Aspirin (M ± m)

No. of suspension	Suspension tested	Single dose of aspirin		Repeated doses of aspirin	
		platelet aggregation, %	accessibility of factor 3, sec	platelet aggregation, %	accessibility of factor 3, sec
1	Platelets of intact rats suspended in blood plasma of same rats	37±2	67,8±1,1	35±1	69,2±2,2
2	Platelets of intact rats suspended in blood plasma of rats receiving aspirin	24±1*	70,0±0,8	22±1*	73,0±2,5
3	Platelets of rats receiving aspirin suspended in blood plasma of the same rats	16±1*,†	70,7±0,8*	22±1*,†	69,2±2,0*
4	Platelets of rats receiving aspirin suspended in blood plasma of intact rats rats	27±1*,†	67,5±1,0†	29±1*,†	69,2±2,0†

*P < 0.05 compared with control suspension 1.
†P < 0.05 compared with preceding suspension.

The aggregating power of the platelets was reduced equally after a single or repeated doses of aspirin, whereas the accessibility of platelet factor 3 was reduced by a greater degree after repeated administration of aspirin.

Comparison of suspensions 1 and 2 shows that the blood plasma of the rats receiving aspirin caused a decrease in the aggregating power of the platelets of the intact animals, and a tendency also was observed for the accessibility of factor 3 of the intact platelets to be reduced. The greatest depression of the functional properties of the platelets was observed in suspension 3, when both platelets and plasma were taken from animals receiving aspirin. Comparison of suspensions 3 and 4 shows that the blood plasma of the intact rats increased the aggregating power and accessibility of platelet factor 3 from animals receiving aspirin. The indices of aggregation and of accessibility of platelet factor were thus at their highest when platelets and plasma were mixed from intact animals; they were lowest when platelets and plasma were taken from rats receiving aspirin; suspensions for which one component (either platelets or plasma) was taken from intact rats and the other from animals receiving aspirin occupied an intermediate position.

It can be concluded from these observations that depression of the functional properties of the platelets following administration of aspirin is due to the effects of the drug on both the platelets and the plasma factors. The transfer of aspirin from the blood plasma of rats receiving aspirin to platelets of intact animals is ruled out, for 24 h after administration of aspirin no salicylates could be found in the blood plasma either in these experiments or by other workers [8]. The possible mechanism of the action of aspirin is by acetylation of the platelets and proteins of the blood plasma [6, 7].

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