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OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

DERMCIDIN ISOFORM-2 INDUCED NULLIFICATION OF THE EFFECT OF ACETYL SALICYLIC ACID IN PLATELET AGGREGATION IN ACUTE MYOCARDIAL INFARCTION

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INTRODUCTION

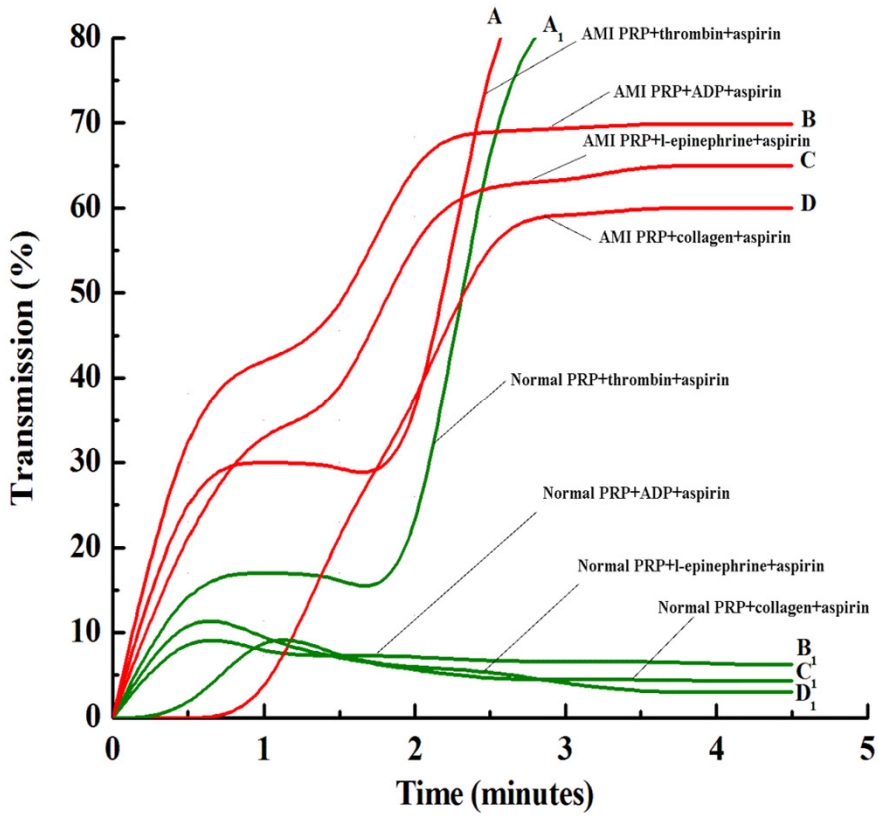
- Acute myocardial infarction (AMI) like other forms of acute coronary syndromes (ACS) is pathophysiologically related to thrombosis that produce infarcts (black patchy) on the pericardium. However, unlike in the case of ACS, the platelet aggregation, induced by different aggregating agents in AMI cannot be inhibited by aspirin (acetyl salicylic acid).

- Currently, there is no known mechanism of platelets in AMI to become resistant to the well known inhibitory effect of aspirin. It is believed that the aggregation of platelets in AMI cannot be inhibited by aspirin, the recurrence of AMI may follow within months and the victims usually succumb to the condition.

- In this presentation, I would present the role of a stress induced protein isolated from the circulation of AMI patients, identified to be dermcidin isoform-2, an 11 kDa small protein and I would also present its role on the development of resistant of platelets to aspirin.

- I would present here unique and a simple way to resensitize the platelets from AMI subjects to the inhibitory effect of aspirin through the expulsion of bound dermcidin from the platelet surface through the increase production of nitric oxide by using low amount of aspirin itself, which unlike the classical inhibition of cyclooxygenase activity through the inhibition of prostaglandin.

Effect of acetyl salicylic acid (aspirin) on the ADP and other platelet aggregating agents induced platelet aggregation in PRP from normal volunteers and from AMI subjects



A = The aggregation of platelets by thrombin (1.0 Unit/ml) in AMI subjects treated with aspirin.
A_1= normal PRP with aspirin on the aggregation induced by thrombin.

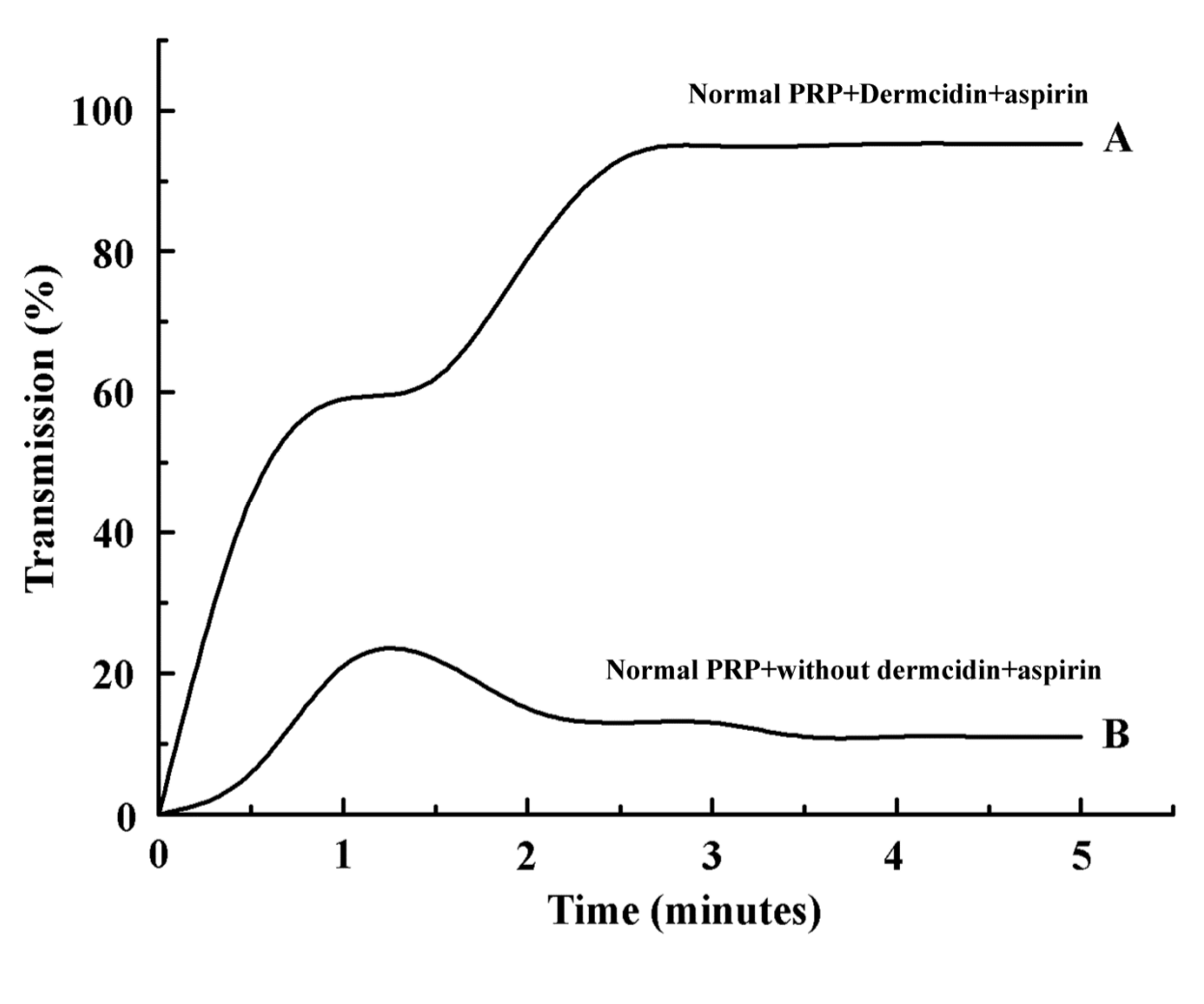
B = The aggregation by ADP (2.0 µM) in AMI subjects treated with aspirin.
B_1=normal PRP with aspirin by ADP.

C = The Aggregation by *l*-epinephrine (5.0 µM) with aspirin AMI subjects.
C_1=normal PRP with aspirin by *l*-epinephrine

D = The aggregation by collagen (2 µg/mL) with aspirin in AMI subjects.
D_1 = normal PRP with aspirin by collagen.

Please note that aspirin can not inhibit aggregation in AMI PRP

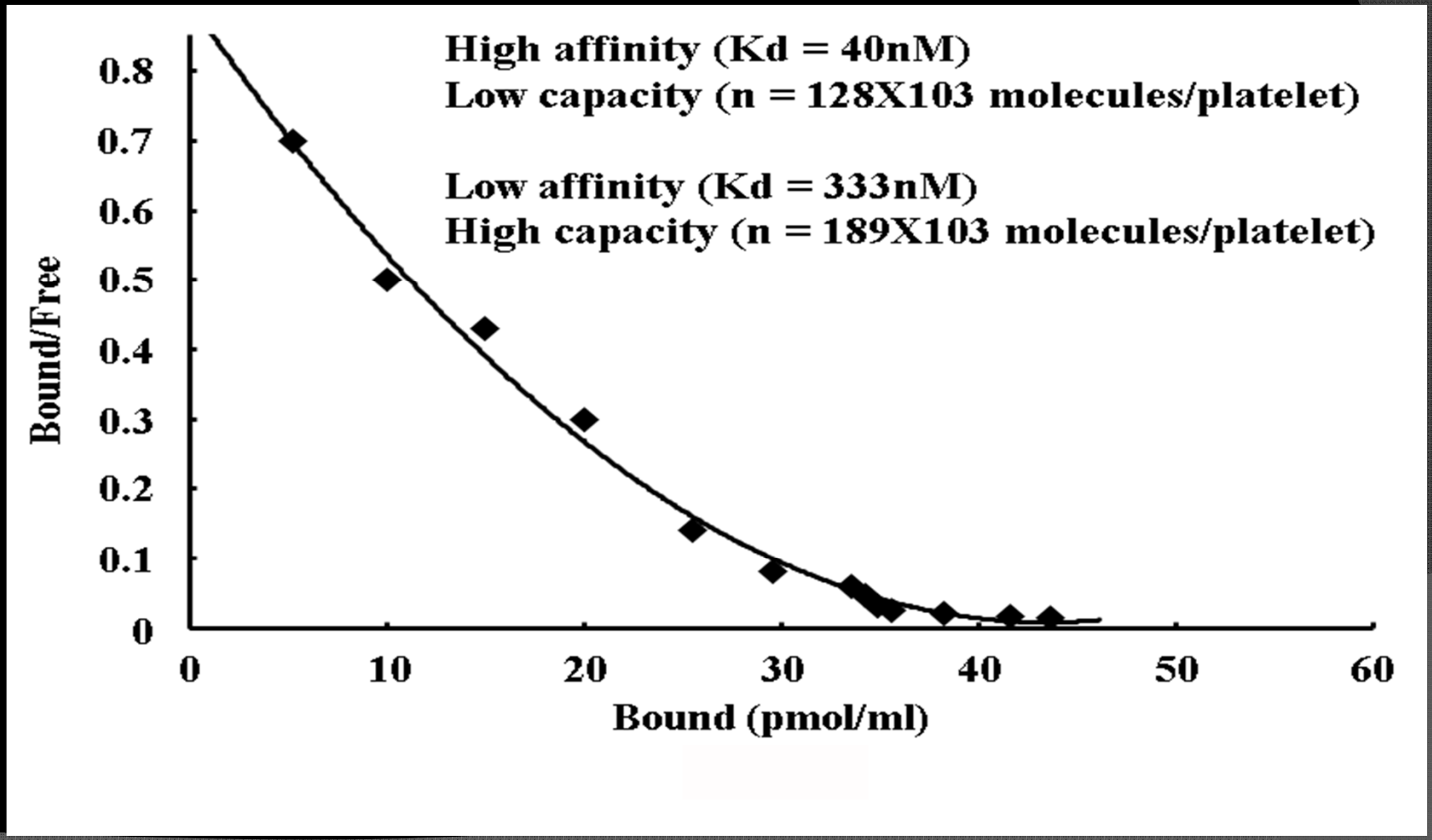
To understand what caused aspirin to fail to inhibit aggregation in AMI subjects



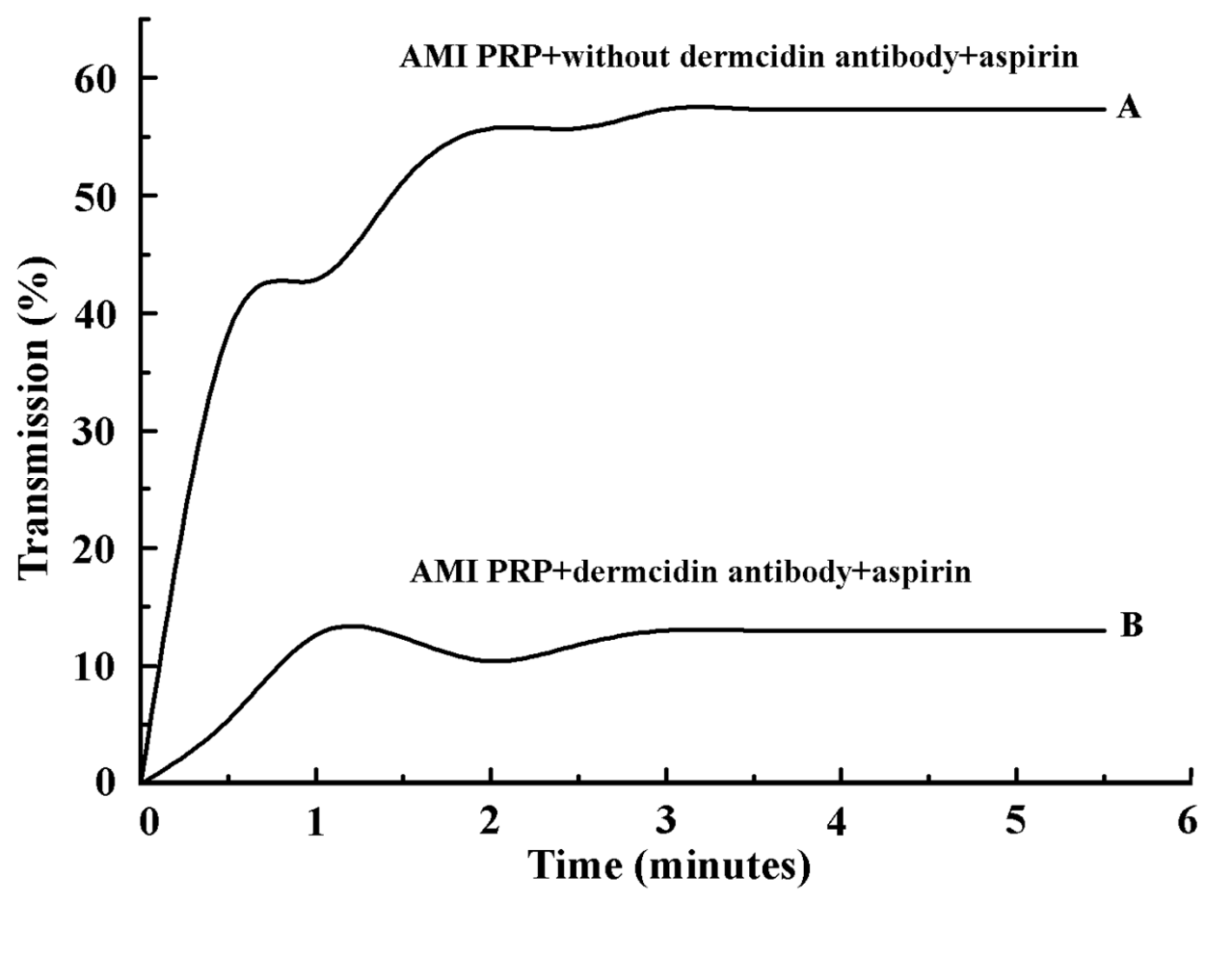
(A) = ADP induced platelet aggregation in the dermcidin treated normal PRP in presence of 80µM aspirin

(B) = ADP induced platelet aggregation in normal PRP not treated with dermcidin in presence of 80µM aspirin.

Scatchard plot analysis of the equilibrium binding of dermcidin to normal platelets



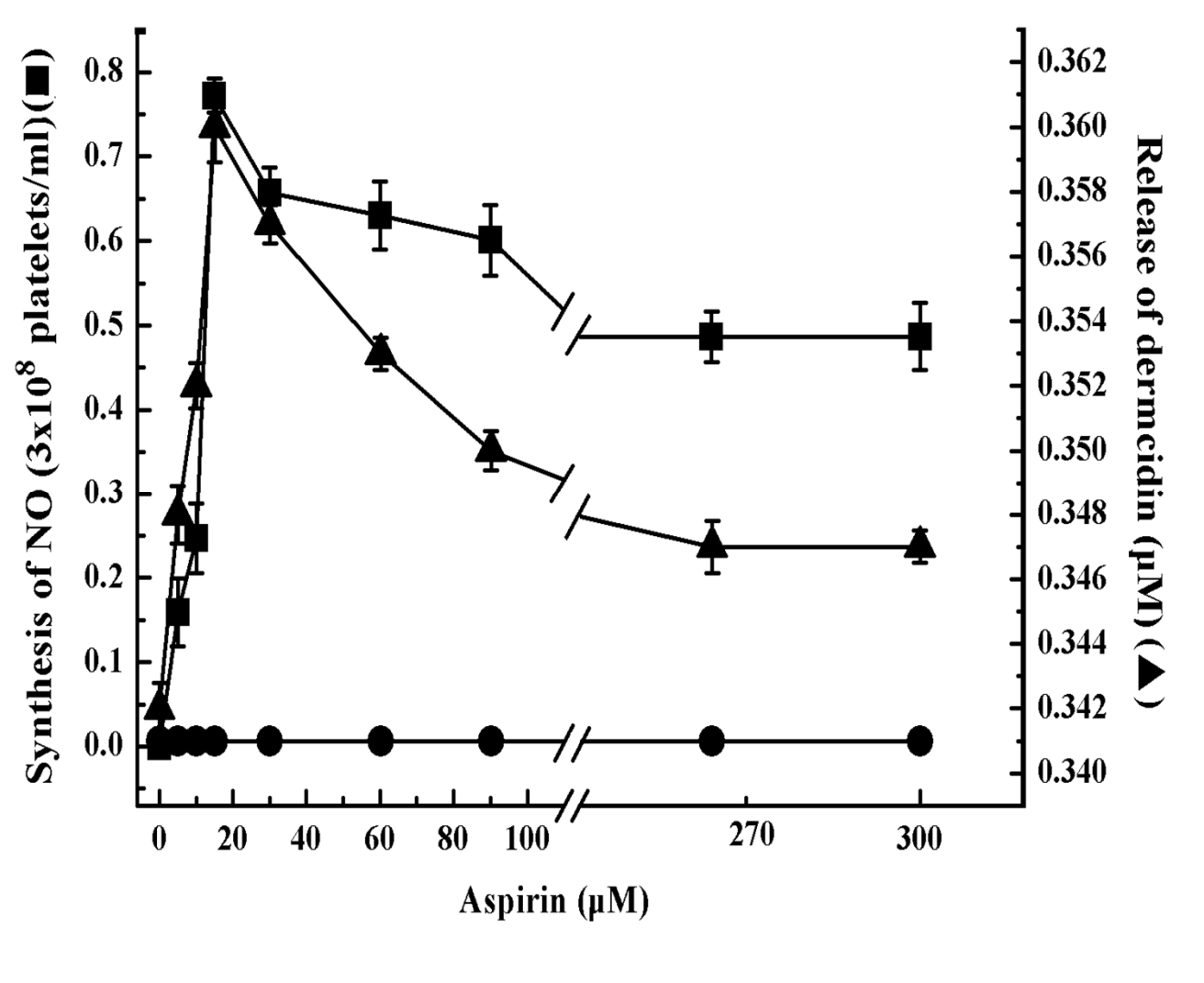
Effect of incubation of PRP from AMI subjects with dermcidin antibody and the inhibitory effect of aspirin on the antibody treated platelet rich plasma.



(A) PRP from AMI subjects was incubated with aspirin and aggregation induced by ADP.

(B) PRP from same AMI patients treated with dermcidin antibody and subsequently treated with aspirin under identical condition like A.

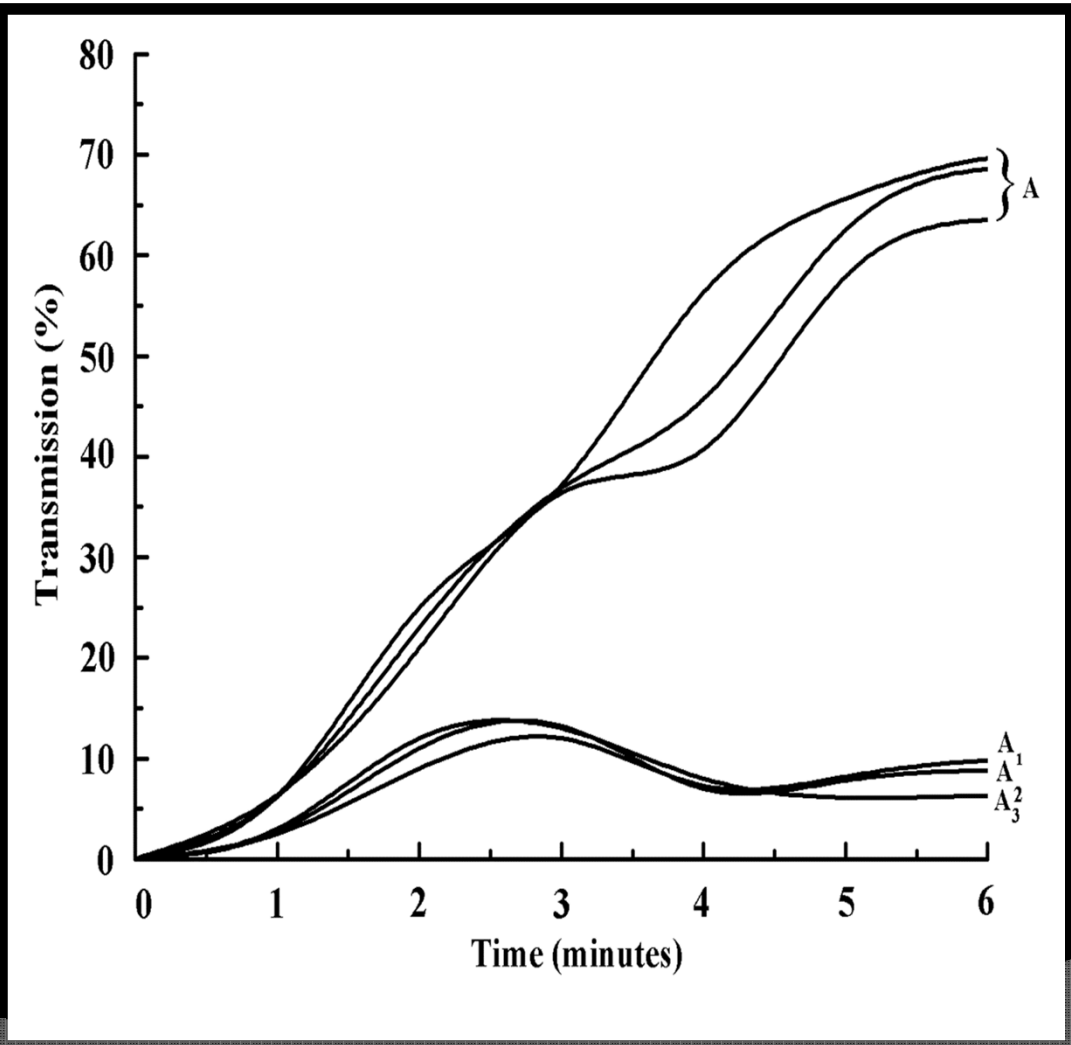
The removal of the bound dermcidin from platelets from AMI subjects by the stimulation of NO in platelets



After the expulsion of bound dermcidin from the AMI PRP, platelet become supersentized.

NAME (solid circles) inhibits the activity of aspirin

Effect of reexposure of PRP from the AMI subjects to 10 µM aspirin on the inhibition of ADP induced platelet aggregation in the PRP pre-treated with aspirin or insulin or NO in 0.9% NaCl.



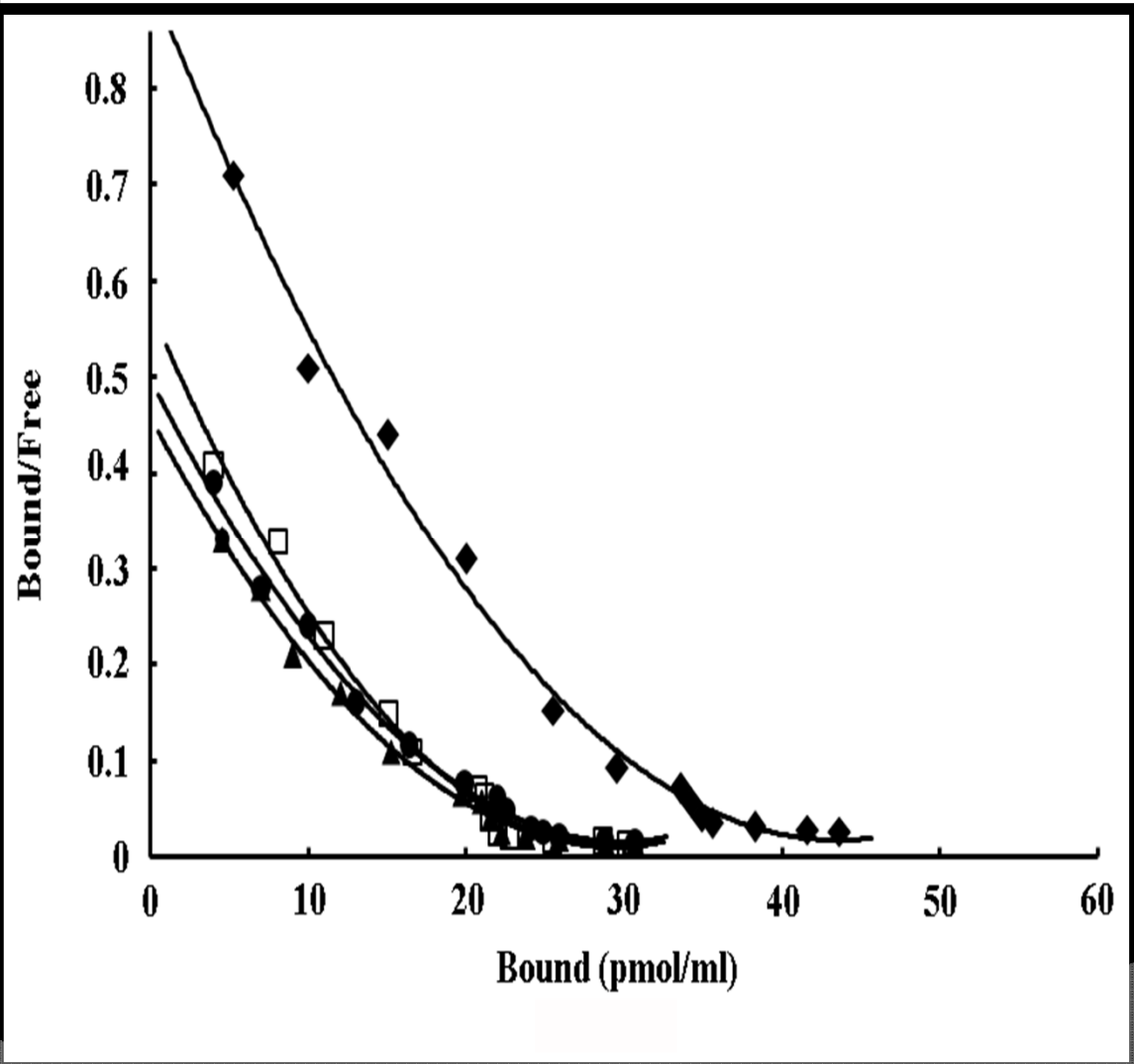
(A)represents the aggregation of platelets in PRP from AMI subjects incubated with 80 µM aspirin

A_1 = The PRP from the same AMI subjects preincubated with 15 µM aspirin followed by treatment of the PRP with 10µM aspirin

A_2 = The PRP from the same AMI subjects was incubated with insulin followed by using 10µM aspirin as.

A_3 = The PRP from the same AMI subjects was incubated with NO solution in 0.9% NaCl followed by using 10µM aspirin.

The effect of preincubation of AMI PRP with aspirin, insulin or with NO in 0.9% NaCl solution on the binding characteristics of dermcidin to platelets in Scatchard plot



It was found that the binding of dermcidin $128X10^3$ molecules/platelet in the untreated AMI platelets decreased to $80X10^3$ molecules/platelet and to $76X10^3$ molecules/platelet and to $78X10^3$ molecules/platelet dermcidin binding sites when the AMI platelets were treated with aspirin, insulin and NO respectively

CONCLUSION

- **The presence of dermcidin in the circulation of AMI impaired the aspirin induced inhibition of platelet aggregation.**
- **These results suggest a novel way to treat the AMI via the resensitization of the platelets to aspirin through the generation of NO.**
- **The increase of platelet of NO level by aspirin, insulin or by NO itself resulted in the removal of the bound dermcidin from its high affinity binding sites on the platelet surface.**
- **The aspirin stimulated NO synthesis in AMI platelets may have a biphasic effect in that the maximal synthesis of NO that will achieved at 15µM of the compound, and the use of higher doses of the compound actually will result in the decrease production of NO, and at 300 mg aspirin/70 kg body weight (equivalent to 333 µM aspirin) will reduce the synthesis of NO with corresponding reduction removal of the platelet bound dermcidin.**

- **If these results from *in-vitro* study could be extended to the subjects affected by AMI, it might be suggested that the use of the 300 mg aspirin is not the optimal dose which could be indeed harmful.**

- **Our preliminary data suggested that perhaps the chronic use of 14 mg bolus of aspirin/70 kg body weight and after 30 min another 9 mg bolus of aspirin/70 kg weight might be helpful in expulsion of platelet bound dermcidin to inhibit aggregation and prevent from the recurrence of AMI.**

THANK YOU

Thanks' for your kind attention!!!!!!



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