

Macrophage activity regulation by high dilution of aspirin and its possible mechanism

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Background: Under LPS-stimulus, platelets can activate macrophage by a cell-to-cell contact or through cytokine degranulation. Rebound effects of anti-thrombotic agents, such as prostanoids and COX inhibitors can lead to thrombosis, infarct, and stroke. Aspirin has been prescribed for decades due to its powerful antiplatelet action, but it is also related to paradoxical effects such as withdrawal syndrome peaks, resistance, and thrombogenesis. Ultra-diluted aspirin can also produce the same effect in one hour, regardless of Cox-2, by still unknown pathways. Antithrombotic effects of aspirin are also reversed by its high dilutions. **Aims:** This study aims to characterize the effects of aspirin 15cH on macrophages challenged with LPS, a Cox-2 activator. **Methodology:** RAW 264.7 macrophages were sown in 24 wells plates using R10 medium, boosted with 1µg/ml LPS and treated with aspirin 15 cH and controls. The activity was evaluated after 24 hours. Supernatants were evaluated for cytokines, nitric oxide, and dielectric oscillations, through solvatochromic dyes (Cartwright's method). **Results and discussion:** macrophage spreading was increased by aspirin 15 cH, a LPS-like effect. Paradoxically, significant reduction of this effect was noted when both, LPS and aspirin 15 cH, were added. Succussed water reversed the effect of LPS, leading to TNF (p<0.05) production close to baseline levels. Also, the single treatment with succussed water inhibited IL-10 production (p<0.05), but aspirin 200 µg/mL (positive control) highly increased it (p<0.0001), showing the validity of the model. Nitric oxide production was strengthened by LPS presence (p<0.0001), as expected, but partially downregulated after treatment with aspirin 200 µg/mL, water and succussed water. A pilot study with solvatochromic dyes showed no significant difference among treatments. **Conclusion:** The main data suggest that aspirin 15 cH increases macrophage activity but presents a paradoxal effect when mixed with LPS. On the other hand, succussed water itself has modulatory effects on macrophages.

Keywords: LPS, homeopathy, solvatochromic dyes, cytokines, NO