BILIVERDIN INHIBITS fMLP AND HEME-INDUCED HUMAN NEUTROPHIL MIGRATION

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Hemolytic disorders can lead to high levels of free heme. Once released heme can aggravate cell damage by free radical generation and membrane desestabilization besides triggering an inflammatory response. One of the heme pro-inflamatory responses is the induction of neutrophil migration *in vivo* and *in vitro*. Biliverdin, the first product of heme degradation, is known as a potent antioxidant and has immunomodulatory properties that were recently described. In this work we investigate the ability of biliverdin to inhibit neuthrophil migration towards a chemotatic stimuli such as heme and fMLP. For *in vitro* studies, cells were pre-incubated with different concentrations of biliverdin for 2 hours and them chemotaxis toward heme or fMLP was assayed using 5 µm polycarbonate membrane for 2 hours. Following incubation, migrated neutrophils were collected, counted on Neubauer chambers and chemotatic index was calculated. For *in vivo* studies, mice were pre-injected i.p. with biliverdin and 2 hours later injected i.p. with fMLP or heme. After four hours, animals were killed and differential counts in the peritoneal fluid were determined. Our *in vivo* and *in vitro* studies demontrate that biliverdin inhibits neutrophil migration towards fMLP or heme suggesting a new anti-inflamatory role for this molecule. Further investigations are in process to unmask the molecular mechanisms involved in such process.

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