Bacterial endotoxin stimulates macrophages / monocytes to release various cytokines early (e.g., TNF-α, IL-1β, and IFN-γ) and late (HMGB-1) which then mediate sepsis (or endotoxemia). HMGB1 recently discovered as late mediator of sepsis, is now seen as one of main mediator of sepsis lethality and prompting investigations for development of new drugs. Present study was undertaken to screen some novel target for ameliorating HMGB1 release and investigate their effect in mice model of endotoxemia.

Here we demonstrate that psychosine increases the HMGB1 in primary peritoneal macrophage cells. The psychosine induced HMGB1 may have some interesting role in pathobiology of Krabbe disease.

Aloe-emodin was seen to abrogate HMGB1 release dose dependently in both RAW 264.7 cells and primary peritoneal macrophage cells. The aloe-emodin was observed to attenuate the release of pro-inflammatory cytokines (TNF-α, IL1β) and LPS – induced oxidative stress markers iNOS, HO-1. The aloe-emodin showed protective effect in endotoxemia rescuing mice from endotoxemia lethality. Aloe-emodin also decreased the systemic accumulation of proinflammatory mediators (TNF-α, IL1-β) within hours in endotoxemic mice. Endotoxemia induced multi-organ dysfunction was also ameliorated by aloe-emodin treatment depicted by serum biochemistry (ALT, ALP, BUN and creatinine) and histopathology of lung, liver and kidney. The neutrophil infiltration was also reduced in lung tissues of aloe-emodin treated mice.

The inhibition of HMGB1 release by aloe-emodin and rescue of endotoxemic mice makes aloe-emodin a potential candidate for sepsis therapy.