Immunomodulatory Properties of 2-Hydroxyethyl Methacrylate

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av

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I. Andersson, J. & Dahlgren, U.I. **Effect of 2-hydroxyethyl-methacrylate (HEMA) on the phagocytic and respiratory burst activity of human neutrophils and monocytes.** *European Journal of Oral Sciences* **116**, 369-374 (2008).

II. Andersson, J. & Dahlgren, U. **HEMA enhances IgG1 production by human B-cells *in vitro*.** *Journal of Dental Research* **89**, 1461-1464 (2010).

III. Andersson, J. & Dahlgren, U. **Effects on mouse immunity of long-term exposure *in vivo* to minute amounts of HEMA.** *European Journal of Oral Sciences* **119**, 109-114 (2010).

IV. Andersson, J. & Dahlgren, U. **HEMA promotes IgG but not IgM antibody production *in vivo* in mice.** Accepted for publication in *European Journal of Oral Sciences*.

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Abstract

Immunomodulatory Properties of 2-Hydroxyethyl Methacrylate

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Professionals working in dentistry have reported adverse effects, such as allergic contact dermatitis, following exposure to 2-hydroxyethyl methacrylate (HEMA). Furthermore unpolymerized HEMA monomers leaking from cured fillings can reach the dental pulp, where HEMA could come into contact with leukocytes.

The aims of this thesis were to study specific effects of HEMA exposure on the phagocytic and respiratory burst activity of human phagocytes (study I), human immunoglobulin production (study II), antibody production (study III, study IV), leukocyte proliferation and leukocyte cytokine production (study III, study IV).

Using fluorescently labeled *Escherichia coli* it was demonstrated that HEMA does not impair the phagocytic activity of either monocytes or neutrophils *in vitro*. By using dihydrorhodamine, a substrate for hydrogen peroxide, it was further shown that HEMA exposure decreases neutrophil respiratory burst activity and thus impairs the bactericidal capacity.

By exposing pokeweed stimulated human B cells to HEMA for six days *in vitro* it was shown that HEMA specifically increases the production of the immunoglobulin IgG1 *in vitro* at lower concentrations, while at higher concentrations HEMA reduces IgG1 and IgM production *in vitro* as well as B cell proliferation. The IgA production *in vitro* appeared insensitive to HEMA exposure.

The effect of long-term exposure to HEMA *in vivo* was analyzed by implanting osmotic pumps, filled with different concentrations of HEMA, subcutaneously in mice. Pumps were left *in situ* for 40 days, during which time the animals were injected with ovalbumin (OVA), dissolved in bicarbonate buffer, on two occasions. Control animals received pumps filled with saline. Mice exposed to high concentrations of HEMA had an impaired weight gain throughout the exposure period and a lower splenocyte interleukin(IL)-2 production *in vitro*. Mice exposed to low concentrations of HEMA had an impaired weight gain in the beginning of the exposure period and lower concanavalin A stimulated splenocyte proliferation *in vitro*, splenocyte IL-2 production *in vitro* and serum IgA anti-OVA antibody activity, compared to control mice.

The *in vivo* effect of HEMA was further studied by injecting mice subcutaneously with HEMA dissolved in bicarbonate buffer, in the presence or absence of OVA. Mice exposed to HEMA, on two separate occasions, had a reduced splenocyte tumor necrosis factor alpha production *in vitro* compared to control animals injected with only buffer. Further both baseline and concanavalin A stimulated splenocyte proliferation *in vitro* was higher compared to controls. Mice exposed to HEMA and OVA in bicarbonate buffer had a higher IgG anti-OVA antibody activity relative to the corresponding IgM anti-OVA antibody activity, compared to animals that were injected with only OVA in buffer.

In conclusion our results suggest that HEMA can suppress as well as enhance immunological responses, specifically affecting neutrophil bactericidal function, immunoglobulin/antibody production, cytokine production and leukocyte proliferation.

Key Words: 2-Hydroxyethyl Methacrylate; Granulocyte; Respiratory burst; Immunoglobulin; B cell; Interleukin; Mouse

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