Immunosuppressive activity of an isoxazolo[5,4-e]triazepine – compound RM33. I. Effects on the humoral and cellular immune response in mice

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Abstract:
The aim of this investigation was to evaluate immunotropic properties of a new isoxazolotriazepine (compound RM33) in mice. We found that RM33 significantly inhibited induction of the humoral immune response to sheep red blood cells (SRBC), given 2 h prior to immunization. The development of the cellular immune response (delayed type hypersensitivity – DTH) to SRBC and to ovalbumin (OVA) was also suppressed, as well as the effector phase of the DTH to OVA. The compound was also effective when administered per os. The suppressive effects of RM33 on the immune response were comparable to those of cyclosporine A (CsA). We also showed that RM33 inhibited DTH to OVA if admixed with the sensitizing dose of an antigen and complete Freund’s adjuvant (cFa) suggesting that the compound may affect initial events of antigen presentation. Such a hypothesis was supported by finding that RM33 significantly inhibited foot pad edema elicited by administration of cFa. The effects of RM33 on the activities of cytokines relevant to development and control of the immune response and inflammation such as: tumor necrosis factor alpha (TNF-α), interleukin 6 and 10 (IL-6 and IL-10) were also studied. The compound markedly (by 63%) inhibited lipopolysaccharide (LPS)-induced TNF-α serum level whereas IL-6 activity was lowered to a lesser extent (by 17%). The inducible IL-10 level in the splenocyte cultures was not affected at all. In summary, the presented results revealed immunosuppressive properties of RM33, which could be associated with its selective interference with co-stimulatory signals provided by adjuvant at initiation of the immune response.

Key words:
isoazolotriazepines, immunosuppression, humoral, cellular immune response, mice, cytokines