

**ENDOCANNABINOID CONGENER  
N-STEAROYLETHANOLAMINE REGULATION  
OF INFLAMMATORY PROCESSES**

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Endocannabinoid system is a recently identified signalling system which is involved in several physiological processes and diseases. A growing body of evidence suggests that endocannabinoid signalling plays critical role in pathogenesis of some inflammatory diseases. While acute inflammation is a part of the defense response, chronic inflammation can lead to cancer, diabetes, cardiovascular and neurological diseases. Endocannabinoids with unsaturated acyl chain (anandamide, 2-acylglycerol) possess protective properties and are known to inhibit the inflammatory response on many effectors. The influence of endocannabinoid congener N-stearoylethanolamine (NSE) on inflammatory process is unknown. The anti-inflammatory effect of NSE on the immediate (anaphylaxis) and delayed type hypersensitivity responses and the inflammation induced by experimental burn was studied.

It was shown that near 70% of guinea pigs in the group which received NSE survived under anaphylaxis. NSE prevented the increase of histamine content in heart, kidney and spleen. NSE also delayed the accumulation of  $\text{NO}_2^-$  - the stable NO metabolite in these organs. At the same time NSE changed to normal the level of nitrite anion in liver and lung and cause the decrease of inducible NO synthase (iNOS) and constitutive NO synthase (cNOS) activity. NSE normalized the content of TBA-reacting compounds in lung and diminished it in heart. NSE prevented the decrease of catalase, superoxide dismutase and glutathione peroxidase activity under anaphylaxis in a dose depended manner.

NSE inhibited by 10 fold the intensity of delayed type hypersensitivity in mice. NSE normalized  $\text{NO}_2^-$  content in blood plasma and in the thymus of sensitized mice.

When studying the mechanism of anti-inflammatory effect of NSE rats after a measured thermal burn of skin received daily *per os* 10 mg/kg of NSE water suspension within 7 days. In another group of rats the NSE suspension (10 mg/ml) was applied on the burning wound. It was shown for the first time that NSE accelerated the process of burn wound healing. NSE inhibited proinflammatory cytokines ( $\text{TNF}\alpha$ , IL-1, IL-6) production and prevented the changes of amino acid content that usually developed as a result of burn. NSE caused the normalization of the iNOS and cNOS activity and of nitrite content in plasma, erythrocytes, liver and spleen of rats. NSE also modified the antioxidant enzymes (catalase, superoxide dismutase and glutathione peroxidase) activity and diminished the level of lipid peroxidation. The discovered anti-inflammatory NSE properties suggest the possibility of its usage for inflammatory processes treatment.